Retinoinvasive Uveal Melanoma: Report of 2 Cases and Review of the Literature

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Keywords

Choroidal melanoma · Retinoinvasive melanoma · Ocular cancer

Abstract

Purpose: To describe the clinical history and histopathologic findings of 2 cases of retinoinvasive uveal melanoma.

Methods: The medical records and pathology specimens of 2 patients with retinoinvasive uveal melanoma were reviewed. **Results:** The first patient had an iris/ciliary body melanoma that was treated and the second patient had suspected iridocorneal endothelial syndrome. Both patients developed a blind, painful eye; the first patient's right eye was enucleated and the left eye of the second patient underwent evisceration. Histopathologic examination of the enucleated eye showed a tumor composed of minimally pigmented spindle-shaped cells with fusiform nuclei and prominent nucleoli and round cells with prominent nucleoli. The tumor cells invaded into the retina where they formed perivascular aggregates. Examination of the evisceration specimen showed a proliferation of pigmented tumor cells within the stroma of one iris leaflet. The tumor cells extended onto the ciliary body and vitreous base and invaded the retina. The

pathologic diagnosis in both patients was retinoinvasive uveal melanoma. **Conclusions:** Careful fundoscopic and imaging examination should be performed in eyes with unilateral glaucoma with iris/ciliary body lesions, and enucleation, rather than evisceration, should be performed, as retinoinvasive melanoma is in the differential diagnosis.

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Introduction

Retinoinvasive melanoma is a rare subtype of uveal melanoma which is characterized by melanoma invasion of the retina at a site noncontiguous with the uveal tumor; this uveal melanoma typically arises in the iris/ciliary body [1]. This melanoma rarely involves the choroid and may exhibit optic nerve invasion [1]. This unusual variant occurs in approximately 0.4% of all eyes enucleated with uveal melanoma [2]. We recently evaluated 2 eyes with retinoinvasive melanoma; one eye from a patient with known iris/ciliary body melanoma had been enucleated; the other eye was eviscerated from a patient with a clinical diagnosis of iridocorneal endothelial (ICE) syndrome.

Fig. 1. Case 1. Gross examination of the enucleated eye shows slight enlargement of the ciliary body (white arrow) and pigment on the posterior corneal surface (black arrow).

Fig. 2. a Case 1. Photomicrograph of the finding seen in Figure 1. A tumor is present in the ciliary body (marked with an asterisk) and on the posterior corneal surface (black arrow). There are also tumor cells on the iris. The anterior chamber angle is obliterated and the tumor infiltrates the trabecular meshwork. **b** Case 2. Melanoma cells are present in the iris (white arrow) and extend into the vitreous base (black arrow). There are lens remnants, and a posterior chamber intraocular lens (marked with an asterisk) is also present. Hematoxylin and eosin. $\times 25$.

Fig. 3. Case 1. Melanoma is present on the retinal surface (black arrow) and has invaded into the retina (white arrow). Hematoxylin and eosin. $\times 100$.

Fig. 4. Case 2. Melanoma is present on the retinal surface and has invaded into the retina. Hematoxylin and eosin. $\times 100$.

Case Reports

Case 1

A 57-year-old woman was evaluated at the Emory Eye Center for pain and redness in her right eye. She had an ocular history of an iris/ciliary body melanoma that had been treated 18 years prior to examination by resection, and 2 recurrences at 11 and 4 years prior to examination were treated with I¹²⁵ plaque brachytherapy. The patient also had a history of pseudophakic bullous keratopathy that had been treated with Descemet stripping endothelial keratoplasty 2 years prior to presentation. At presentation, her best-corrected vision was light perception, and the intraocular pressure (IOP) was 21 mm Hg. Slit-lamp examination showed a corneal infiltrate, which was scrapped and cultured and proved to be fungal keratitis. The fungal keratitis was treated and resolved. An ultrasound was performed after resolution of the keratitis which showed an iris/ciliary body mass that measured 1.2 mm in thickness. A re-measurement 3 months later showed the mass to measure 2.2 mm in thickness. Six months later, the IOP had increased to 40 mm Hg, and the slit-lamp examination remained unchanged.

She was treated with topical IOP-lowering drops, and after an additional 6 months, the patient requested enucleation of her blind, painful right eye. Gross examination of the enucleated eye showed a minimally visible tumor in the ciliary body and pigment on the posterior corneal surface (Fig. 1). Histopathologic examination of the enucleated eye showed a tumor involving the iris, anterior chamber angle, trabecular meshwork, and posterior corneal surface (Fig. 2a). The tumor was composed of minimally pigmented spindle-shaped cells with fusiform nuclei and prominent nucleoli and round cells with prominent nucleoli. These tumor cells formed membranes and focal aggregates on the inner retinal surface. The tumor cells invaded into the retina (Fig. 3) where they formed perivascular aggregates. Tumor cells also invaded the optic nerve head. The diagnosis was retinoinvasive melanoma.

Case 2

A 44-year-old man had cataract surgery with an intraocular lens implantation on his left eye. He was diagnosed with ICE syndrome many years prior to the current evaluation and had been treated with Descemet stripping endothelial keratoplasty. He had

Table 1. Literature review of clinical and histological features of retinoinvasive uveal melanomas

Authors, year [Ref.]	Patient data		Clinical features				Histology features		
	sex	age, years	previous treatment	tumor type	glaucoma/ OHT	time to enucleation, years	cell type	optic nerve invasion	extrascleral extension
Terry, 1940 [4]	F	53	no data	ring melanoma	yes	3	mixed	retrolaminar, chiasmal extension	yes
Spencer and Iverson, 1965 [5]	M	56	no	ring melanoma	yes	12	mixed, necrotic	retrolaminar	no
Spencer, 1975 [6]		76	no	ring melanoma	yes	no data	necrotic	retrolaminar	no
Kivelä and Summanen, 1997 [1]	F	74	cryotherapy, iridocyclectomy	ring melanoma	yes	9	mixed	retrolaminar	yes
Milman et al., 2012 [2]	F	69	plaque brachytherapy	choroidal melanoma	yes	2	mixed	retrolaminar	yes
	M	63	plaque brachytherapy	no data	yes	6	epitheloid	retrolaminar	no
	F	59	proton beam irradiation	no data	no	1	mixed	prelaminar	no
	M	79	plaque brachytherapy	no data	yes	11	mixed	no	no
Present study, 2016	F	57	iridocyclectomy, plaque brachytherapy, DSEK for PBK	iris/ciliary body melanoma	yes	19	mixed	prelaminar	no
	M	44	DSEK for suspected ICE syndrome	iris/ciliary body melanoma	yes	evisceration (unsuspected intraocular tumor)	mixed	no data	no data

DSEK, Descemet stripping endothelial keratoplasty, PBK, pseudophakic bullous keratopathy, ICE, iridocorneal endothelial.

therapy-resistant glaucoma and his left eye became increasingly painful. He was referred to an oculoplastic surgeon for intermittent pain in his left eye for many years. The evaluation showed that this best-corrected visual acuity was hand motions and the IOP was 10 mm Hg. Slit-lamp examination showed an opaque cornea. The patient underwent evisceration of his blind, painful left eye. Examination of the evisceration specimen showed a proliferation of pigmented tumor cells within the stroma of one iris leaflet. The tumor cells extended onto the ciliary body and vitreous base (Fig. 2b). The tumor extended onto the inner retinal surface as well as invaded the retina (Fig. 4). Immunohistochemical stains were positive for HMB-45 in the tumor cells. The diagnosis was retinoinvasive melanoma.

Discussion

An analysis of 232 eyes with choroidal melanoma showed retinal invasion around the site of the tumor in 59% of cases [3]. Retinoinvasive uveal melanoma, described by Kivelä and Summanen [1] in 1997, is a phenotype of uveal melanoma in which the tumor is present in the iris and/or ciliary body and invades the retinal via transvitreal extension distant to the primary tumor. This

subtype is thought to be a late presentation of uveal melanomas. A retrospective review of pathology records from 3 tertiary referral centers showed invasion of the inner retina from a site distinct from the primary tumor in only 0.4% of eyes enucleated for uveal melanoma [2].

Cases of retinoinvasive uveal melanoma described in the literature have common clinical and pathologic features (Table 1). There have been 8 previously reported cases [1, 2, 4–6]. The age range of these patients is 53–79 years, and men and women are equally affected. These tumors involve the iris/ciliary body and may grow in a “ring melanoma” fashion in the ciliary body [1, 4–6]. The mean time from presentation to enucleation is approximately 8 years, highlighting the indolent, slowly progressive nature of these tumors. Most patients with retinoinvasive uveal melanoma have increased IOP, invasion of the optic nerve, and retrocorneal involvement [1]. They infrequently have choroidal involvement [1]. Both of our cases had a primary iris/ciliary body melanoma which exhibited transvitreal invasion of the retina at a distant site. Both of our patients had increased IOP, with the second patient carrying a diagnosis of ICE syndrome. Our first

patient had retrocorneal spread and optic nerve invasion of the melanoma. In this case, the melanoma cells invaded through the retina, and they spread along the inner limiting membrane to the optic nerve head until reaching the lamina cribrosa. Neither of our cases exhibited choroidal involvement of the melanoma.

Our first patient had a clinical diagnosis of melanoma and underwent enucleation. Our second patient had a clinical diagnosis of ICE syndrome and his left eye underwent evisceration. Lee et al. [7] noted that melanoma along the corneal endothelium, especially in the setting of refractory glaucoma, may be misinterpreted as ICE syndrome. Melanoma cells spreading on the posterior surface of the Descemet membrane may block the anterior chamber angle and Schlemm's canal causing secondary glaucoma. Unsuspected uveal melanoma has also been found in eyes eviscerated for endophthalmitis, phthisis bulbi, and nonclearing vitreous hemorrhage [8]. In some of the cases described by Eagle et al. [8], melanoma was not suspected prior to enucleation, even with preoperative ultrasonography. Based on previous reports, Kivelä and Summanen [9] concluded that besides ciliary body melanoma other anterior segment neoplasms could show retinoinvasive features.

Retinoinvasive uveal melanoma is challenging to diagnose clinically and may be diagnosed only by histopathologic examination of an enucleated eye. Elevated IOP and a prior diagnosis of iris/ciliary body melanoma are clues to the diagnosis. Although posterior segment visualiza-

tion may be challenging in such patients, careful fundoscopic examination and imaging (ultrasound/optical coherence tomography) are needed to exclude an occult retinoinvasive uveal melanoma. One must have a high index of suspicion for melanoma in blind, painful eyes refractory to glaucoma therapy, such as in the presumptive ICE syndrome. It is also advisable to submit any iris specimen obtained during filtering surgery for histopathologic evaluation in ICE syndrome to exclude melanoma. Evisceration should only be performed if there is absolutely no clinical possibility of retinoinvasive uveal melanoma.

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Statement of Ethics

The study followed the tenets of the Declaration of Helsinki. The Emory University Institutional Review Board granted exempt status to this study.

Disclosure Statement

The authors declare no conflicts of interest.

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