Acute Presentation of Mesectodermal Leiomyoma of the Ciliary Body

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Established Facts

- Ciliary body mesectodermal leiomyoma is a rare but benign tumor of the eye that can mimic uveal melanoma.
- Previously published cases of mesectodermal leiomyoma presented incidentally or with progressive blurry vision.

Novel Insights

- Mesectodermal leiomyoma can present with acute, painless vision loss.

Keywords

Benign tumor · Melanoma · Immunohistochemistry · Leiomyoma · Enucleation

Abstract

Purpose: We report a case of acutely presenting mesectodermal leiomyoma of the ciliary body in a 29-year-old female who reported waking up with swollen eyelids of the right eye and light-perception vision. The affected eye had elevated intraocular pressure, a flat anterior chamber, and a pale, round mass arising from the nasal ciliary body, invading the angle and protruding into the visual axis posterior to the lens. Within days, the visual acuity decreased to no light perception. The eye was enucleated. **Methods:** The enucleated eye harbored a tumor arising from the ciliary

body, measuring 18 mm in the greatest dimension. Spindled cells with fibrillary cytoplasmic processes suggested a neural origin though negative for S-100, Melan-A, and HMB-45. The cells stained strongly positive for smooth muscle actin and vimentin, leading to the diagnosis of mesectodermal leiomyoma of the ciliary body. **Results:** We review the literature to expand upon the clinical findings, diagnostic methods, and histopathologic and immunohistochemistry characteristics of mesectodermal leiomyoma. **Conclusion:** Leiomyoma must be in the differential diagnosis for ciliary body mass, especially in women of reproductive age. Diagnosis relies on histopathology and immunohistochemistry. The mechanism of acute symptom onset may be multifactorial. This case emphasizes the possibility of acute presentation of a rare, benign intraocular tumor.

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Introduction

Mesectodermal leiomyoma of the ciliary body is a rare, benign tumor of the eye with fewer than 30 reported cases since the first published case in 1977 [1]. This rare type of tumor, presumed to be of neural crest origin, microscopically exhibits both muscular and neural features [2, 3]. It is a subtype of ciliary body leiomyoma, a benign tumor of smooth muscle [3]. Leiomyomas must be differentiated from uveal melanoma because of the vastly different prognosis and management of these entities. Clinically, there is no reliable method of differentiating mesectodermal leiomyoma from uveal melanoma, and the diagnosis relies almost exclusively on histopathology and immunohistochemistry [4–7]. We report a case of a mesectodermal leiomyoma that presented with acute, painless loss of vision in a young Caucasian woman.

Case Report

A 29-year-old Caucasian female with unremarkable personal or family medical history presented to her local emergency department with acute, painless vision loss of her right eye and eyelid swelling. She was unaware of a prior decrease in vision. On examination, she had light-perception vision with intraocular pressure of 60 mm Hg due to secondary closure of the iridocorneal angle and a right afferent pupillary defect by reverse. The superior and inferior eyelids of the right eye were markedly erythematous and edematous. The extraocular motility was marginally limited in all directions. Diffuse conjunctival chemosis and corneal edema were noted, and a nasal mass was visualized in the angle despite a flat anterior chamber (Fig. 1a). There was no view to the posterior segment due to the mass. B-scan ocular ultrasound revealed a dome-shaped, acoustically solid mass (18 mm in height, 16 mm in width) growing from the anterior uvea with a small, central anechoic area. Associated retinal detachment was also seen and later correlated to histopathologic findings (Fig. 1b). The mass occupied more than 50% of the globe on the ultrasound and was also seen on the CT scan of the orbits with dislocation of the crystalline lens (Fig. 1c). Initial workup for systemic infectious and inflammatory disease was negative. On the second day of presentation, a transscleral biopsy of the mass was performed by the local ophthalmologists to assess for local infection and immunohistochemistry. Necrotic debris suspicious for glial tissue was surrounded by tissue staining positively for smooth muscle actin, desmin, and vimentin, suggesting smooth muscle origin of the resected area. Infectious agents were not seen on the PAS stain. No conclusion was made based on the small tissue sample. The patient was then transferred to a tertiary care center where the decision was made to enucleate the eye due to the size of the mass and poor visual potential of the eye. She had no-light-perception vision at the time of enucleation, which was performed 5 days after presentation.

On sectioning of the enucleated globe, the mass was measured to be 18 mm in the greatest dimension (Fig. 2a). About 50% of the tumor was necrotic with associated hemorrhage, but the vi-

Fig. 1. Clinical presentation of the ciliary body mesectodermal leiomyoma. **a** Slit-lamp photograph of the right eye. The eye is notable for diffuse conjunctival chemosis and nasal sentinel vessels associated with a mass in the nasal angle. The anterior chamber is flat secondary to the ciliary body mass causing anterior shift of the iris. Note the posterior synechiae that suggest chronic inflammation in the anterior chamber. **b** B-scan ocular ultrasound performed at presentation. The acoustically solid mass arising from the ciliary body has a central anechoic area that corresponds histologically with necrosis. **c** CT of the orbit without contrast. This imaging modality confirms the presence of a large intraocular mass arising from the nasal ciliary body that temporally displaces the crystalline lens and expands the total volume of the globe compared to the fellow eye. Proptosis is appreciated on the image.

able portions of the tumor consisted of spindled cells with fibrillary cytoplasmic processes and indistinct cell boundaries conferring a neural appearance (Fig. 2b). Immunohistochemistry of those cells, however, was negative for all markers of melanoma including S-100, Melan-A, HMB-45, and Sox-10. The tumor cells were, however, strongly positive for smooth muscle actin (Fig. 2c). Vimentin staining was focal and mostly showed a perinuclear pattern (Fig. 2d). No mitoses were seen histologically, and Ki-67 staining showed a proliferative index of <1% (Fig. 2e). This lesion was diagnosed as a mesectodermal leiomyoma of the ciliary body.

Fig. 2. Gross and histopathologic appearance of the mesectodermal leiomyoma. **a** Gross section. A yellowish, solid tumor measuring 18 mm in the greatest dimension arising from the ciliary body. **b** Hematoxylin and eosin stain. The mass consists of cells with indistinct cell borders and round to fusiform nuclei; the cytoplasm has a fibrillary appearance that conferred a neuroid morphology. There is minimal mitotic activity. **c** Immunohistochemistry for smooth muscle actin; the tissue diffusely stains positive. **d** Immunohistochemistry for vimentin. The staining is focal, restricted to the periphery, and with an unusual perinuclear pattern. **e** Immunohistochemistry for Ki-67 (Mib-1). The staining index is very low at 0% in the center of the tumor, focally rising to about 5% in the periphery. Overall, it is <1%. **f** The neurosensory retina is diffusely detached with obvious atrophy of the outer retinal layers and associated serous subretinal fluid. HE, $\times 20$.

Notably, the neurosensory retina was found completely detached with parts folded upon itself (Fig. 2f). Atrophic changes of the outer layers suggested at least a subacute, if not chronic, state of detachment. The mass lesion extended through the sclera at the site of the prior biopsy site (performed 3 days prior to the enucleation), and there was early reactive fibrosis in this area. It was felt that this extension represented protrusion of the tumor through the scleral defect created by the biopsy rather than tumor invasion through the sclera.

Discussion

Mesectodermal leiomyoma is a rare intraocular tumor arising from neural crest cells [1, 7, 8]. The epidemiology shows predilection for women of reproductive age. Of the 30 cases of mesectodermal leiomyoma reported to date including the present case, 22 of them were in women (Table 1). The most common presenting symptom is pro-

gressive decrease in vision related to the mass that most often arises from the ciliary body but also from the iris [9] and choroid [10]. A few cases of leiomyoma presented as anterior staphyloma [11, 12]. Although there is no report of recurrence or metastasis after enucleation, the regrowth of incompletely resected tumors has been reported [13].

Intraocular leiomyomas often grow slowly enough to warrant cautious observation, especially when the clinical suspicion is high and vision is preserved [14]. Rapid growth can be associated with leiomyosarcoma [15], the malignant counterpart of intraocular leiomyoma. Leiomyosarcoma characteristically has a high mitotic rate with significant cytologic atypia, neither of which was seen in this case. Benign leiomyomas do grow over time, however, and can cause complications such as retinal detachment, glaucoma, lens subluxation, and even extra-scleral extension [2]. The tumor presented herein is

Table 1. A list of published cases of mesectodermal leiomyoma on PubMed using the search term “ciliary body mesectodermal leiomyoma”

Case	Year of publication	First author [ref.]	Age, years	Sex	Presenting symptom	OD/OS	Presenting visual acuity	Location of the mass	Greatest dimension, mm	Method of diagnosis or treatment	Duration of follow-up, years	Recurrence or metastasis	Final visual acuity
1	1977	Jakobiec [1]	37	F	Incidental	OS	20/20	Superonasal CB	6	Iridocyclectomy	6	No	20/25
2			20	F	Blurry vision	OD	20/25	Superotemporal CB	9	Enucleation	n/a	No	Enuc
3	1978	Jakobiec [7]	28	F	Blurry vision	OD	20/40	Temporal CB	9	Enucleation	14	No	Enuc
4	1980	Croxatto [18]	23	F	Incidental	OS	20/30	Superonasal CB	14	Iridocyclectomy	1	No	n/a
5	1985	Orsoni [19]	18	F	Blurry vision	OD	4/50	Inferotemporal CB	8	Enucleation	n/a	No	Enuc
6	1985	Takagi [20]	38	F	Visual disturbance	OS	20/50	Superior	13	Enucleation	n/a	No	Enuc
7	1989	Ishigooka [4]	28	F	Self-detected mass	OD	20/50	Inferotemporal CB	8.5	Corneocyclo-iridocyclectomy	8	No	20/30
8	1989	Shields [17]	11	F	Incidental	OD	6/9	Inferonasal CB	14	Iridocyclo-choroidectomy	1 mo	No	6/9
9	1989	Burk [21]	63	F	Dilated pupil	OD	n/a	Inferotemporal CB	6	Resection	n/a	n/a	n/a
10	1989	White [22]	38	M	Incidental	OD	6/12	Inferotemporal CB	8	Cyclectomy	5 mo	No	6/12
11	1990	Yu [23]	8	M	n/a	OS	n/a	Inferotemporal CB	13	Iridocyclectomy	n/a	n/a	n/a
12	1994	Campbell [24]	47	F	n/a	OD	3/200	Temporal CB	22	Enucleation	n/a	n/a	Enuc
13	2002	Perri [6]	23	M	Blurry vision	OS	20/200	Posterior choroid	12	Enucleation	n/a	n/a	Enuc
14	2002	Alenda [25]	37	F	n/a	OS	n/a	Ciliary body	15	Enucleation	n/a	n/a	Enuc
15	2003	Park [13]	19	F	Blurry vision	OD	n/a	Temporal CB	20	Local resection	6	Re-growth	Enuc
16	2004	Lai [5]	23	F	Blurry vision	OS	Hand motion	Inferonasal CB	8	Biopsy	n/a	No	n/a
17	2007	Miyamoto [10]	40	F	Visual field defect	OS	20/100	Posterior choroid	13	Enucleation	1.5	No	Enuc
18	2007	Odashiro [3]	21	M	Enlarging mass	OD	n/a	Inferior	5	Iridocyclectomy	3	No	n/a
19			54	F	Blurry vision	OD	n/a	n/a	9	Enucleation	2	No	Enuc
20	2008	Koletsa [8]	53	F	Blurry vision	OD	20/400	Anterotemporal	12	Enucleation	n/a	n/a	Enuc
21	2009	Sojka [26]	15	F	Blurry vision	OS	n/a	n/a	21.6	Enucleation	n/a	n/a	Enuc
22	2011	Razzaq [2]	20	M	Enlarging mass	OD	20/20	CB	9.7	Excisional biopsy + brachytherapy	n/a	n/a	n/a
23	2012	Chalam [9]	61	M	Blurry vision	OD	20/40	Iris	11.3	Excisional biopsy	n/a	n/a	n/a
24	2013	Quhill [16]	60	F	Blurry vision	OD	n/a	Inferotemporal CB	14.2	Enucleation	n/a	n/a	Enuc
25			66	F	Incidental	OS	n/a	Temporal CB	5.7	Excisional biopsy	n/a	No	n/a
26			55	M	Incidental	OD	n/a	Temporal CB	8	Iridocyclectomy	n/a	n/a	n/a
27	2014	Rentería-Ruiz [27]	35	F	Blurry vision	OD	20/50	n/a	10	Local resection	n/a	n/a	n/a
28	2016	Lavric [12]	15	M	Staphyloma	OD	n/a	Anterior staphyloma	n/a	Enucleation	1	n/a	Enuc
29			31	F	Visual disturbance	OS	n/a	Anterior staphyloma	n/a	Not available	6	n/a	n/a

CB, ciliary body; n/a, not available; mo, months; Enuc, enucleation.

thought to have had a long period of clinical silence during which slow detachment of the peripheral retina correlating with histologic atrophy took place. Concurrently, the patient likely had pervasive secondary angle closure with anterior chamber inflammation leading to posterior synechiae and glaucoma – hence the afferent pupillary defect seen on initial examination. The tumor presumably had outgrown its own vascular supply, evidenced by areas of necrosis and hemorrhage seen microscopically. Inflammation reactive to the necrosis may have contributed to the posterior synechiae and perhaps also to the eyelid swelling seen on the day of presentation. In addition to the clinical evidence of a chronic and progressive course of the tumor, histopathology also argues against the diagnosis of aggressive leiomyosarcoma but rather for mesectodermal leiomyoma based on the low mitotic rate and minimal cytologic atypia¹. The exact mechanism underlying the acute presentation of vision loss is difficult to

pinpoint but may have been multifactorial including poor symptom awareness by the patient. Nonetheless, this case is the first acute presentation of this rare tumor and highlights the possibility of such presentation for this slow-growing, benign tumor.

Leiomyoma may be clinically difficult to distinguish from uveal melanoma. Transmission of light on transillumination has been reported by Shields et al. [11] as a

¹ The diagnosis of leiomyoma versus leiomyosarcoma in this patient is based predominantly on the very low mitotic rate and lack of cytologic atypia. While admittedly clear criteria for separating benign from malignant smooth muscle tumors occurring in the uvea have not been established, owing to the rarity of these lesions, mitotic rate has been shown to be a reliable predictor of malignancy in smooth muscle tumors of the uterus, and cytologic atypia has been shown to be an important distinguishing factor for smooth muscle tumors of the deep soft tissues. Longer follow-up may prove this diagnosis to be wrong if metastases develop in the absence of any other primary site. At present, however, analogy with smooth muscle tumors of other sites suggest that this tumor will have been cured by this resection.

potential distinguishing feature of leiomyoma, which transmits light, compared to uveal melanoma, which blocks light [5]. Large leiomyomas, however, such as the giant leiomyoma reported by Remmer et al. [14] do not obey this rule, blocking transillumination as uveal melanoma would and thus further obscuring the clinical diagnosis of leiomyoma. B-scan ocular ultrasonography can sometimes identify a suprachoroidal location of the tumor to differentiate it from uveal melanoma that arises from the uvea itself [14], but such detail may not always be evident. The B scan in the present case did not elucidate the identity of the tumor as leiomyoma. One report suggests that MRI with gadolinium contrast can be a helpful diagnostic modality to differentiate uveal melanoma from leiomyoma [12], but the consensus is that diagnosis is primarily based on histopathology and immunohistochemistry rather than clinical, ultrasonographic, or radiologic evidence.

Histopathologic characteristics of mesectodermal leiomyoma include neural morphology of cells on light microscopy with immunohistochemistry staining positive for smooth muscle actin, desmin, vimentin, and negative for melanoma stains such as Melan-A and HMB-45 [8]. Some mesectodermal leiomyomas can be S-100 positive, a marker typically associated with melanoma, so this marker should not be used in isolation for diagnosis. Recently, CD56 has been used to confirm the neurogenic characteristics of mesectodermal leiomyoma [3, 5], but this stain adds little to the diagnosis especially when the morphology is convincingly neuroid. By definition, mesectodermal leiomyoma has minimal mitotic activity, which contrasts with leiomyosarcoma characterized by significant mitotic activity seen both on light microscopy and staining for cellular proliferation [12].

Of note, “mesodermal” leiomyomas of the ciliary body, the broader category of tumor within which mesectodermal leiomyoma is a subset, has the same immunohistochemical profile but with more myogenic morphology on light microscopy [3]. For the purposes of clinical characterization, prognostication, and treatment planning, mesectodermal leiomyoma is equivalent to the mesodermal leiomyoma.

The management of leiomyoma can vary from observation to enucleation, and, as advocated more frequently, local resection [11, 12, 16, 17]. Observation is seldom recommended unless the clinical suspicion for leiomyoma is high, which is difficult because of its shared clinical features with uveal melanoma. Considering that growth is certain and morbidity can include glaucoma, retinal detachment, and extrascleral extension as previously

mentioned, surgical management is necessary for both histopathologic diagnosis and treatment. Note that in this case, however, the transscleral biopsy of the lesion was inconclusive, and the visual potential of the eye was low with no-light-perception vision on day 5 of presentation. Management decisions must be made on a case-by-case basis, and enucleation, as in this case, may be justified based on the locally aggressive nature of large tumors.

This case illustrates the importance of histopathologic and immunohistochemical diagnosis of this rare tumor and the possibility of acute presentation. The list of differential diagnoses includes amelanotic uveal melanoma, ciliary body metastases, leiomyosarcoma, neurofibroma, and schwannoma. The microscopic distinction between melanoma and leiomyoma should be confirmed with immunohistochemistry. The low mitotic rate of the tissue differentiates leiomyoma from leiomyosarcoma. The tumor presented herein is large with 18 mm in the greatest dimension and is unique in its acute presentation of vision loss.

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Statement of Ethics

This study was conducted in compliance with the rules and regulations of the Health Insurance Portability and Accountability Act as well as in adherence with the Declaration of Helsinki and all other relevant federal and state laws.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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