Intraocular Schwannoma: Case Series of 28 Patients and Literature Review

Yue-Ming Liu

Beijing Tongren Hospital

Li Dong

Beijing Tongren Hospital

Xiao-Lin Xu

Beijing Tongren Hospital

He-Yan Li

Beijing Tongren Hospital

Qiong Yang

Beijing Tongren Hospital

Rui-Heng Zhang

Beijing Tongren Hospital

Wen-Bin Wei (✉ weiwenbintr@163.com)

Beijing Tongren Hospital <https://orcid.org/0000-0003-2386-0989>

Research

Keywords: Intraocular schwannoma, Choroidal schwannoma, Uveal schwannoma, Case series

Posted Date: September 14th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-864638/v1>

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Abstract

Background: Intraocular schwannoma is a rare intraocular tumor, which is often misdiagnosed. We aimed to analyze the demographics and clinical characteristics of patients with intraocular schwannoma.

Methods: Retrospective case series were collected from May 2005 to July 2021 in Beijing Tongren Hospital. Then a literature review was also performed.

Results: A total of 28 patients were diagnosed with intraocular schwannoma histopathologically. The median age (range) of the included patients was 39 (12-64) years old, among whom half subjects were female. The most common symptom was visual loss (75.0%), followed by visual field loss (10.7%). Intraocular schwannoma presented as nonpigmented mass, which occurred mainly in ciliary body (42.9%), followed by choroid (32.1%) and ciliochoroid (25.0%). 16 patients (57.1%) were clinically misdiagnosed as uveal melanoma. Tumor excision was performed for all patients and increased light transmission was detected in half cases. In the consecutive follow-up (median: 6.0 years, range: 0.5-16.0 years), no recurrence or metastasis case was detected.

Conclusions: Intraocular schwannoma is a rare benign intraocular tumor. It usually presents as nonpigmented mass, which is easily misdiagnosed as nonpigmented uveal melanoma.

Background

Schwannoma, also known as neurilemmoma or neurinoma, is a benign tumor that originates from the peripheral-nerve sheath [1]. Schwannoma is a rarely seen intraocular tumor that occurs in ciliary body, choroid, and occasionally in the iris [2–3]. They are rarely pigmented, while usually amelanotic or pseudo-pigmented when covered by retinal pigment epithelium. However, it is difficult to distinguish schwannoma from amelanotic malignant melanoma by clinical examination alone. To our knowledge, malignant transformation of an intraocular schwannoma has not yet been reported. Although this type of tumor is cytologically benign and not life threatening, appropriate treatment is required to prevent visual loss and its progressive enlargement. In this study, we reviewed our experience dealing with 28 intraocular schwannoma patients, which contains the largest sample size so far. We aimed to describe the clinical features, relevant histopathology, and treatment options of intraocular schwannoma.

Methods And Materials

Data collection

We retrospectively reviewed the clinical data and histopathological materials from all patients with documented intraocular schwannoma, who were diagnosed in Beijing Tongren Hospital from May 2005 to July 2021. Patients' age, sex, symptoms, systemic diseases, tumor locations, preoperative clinical diagnoses, and treatment procedures were all recorded. Hematoxylin-eosin-stained slides were available in all cases, as well as special stains such as periodic acid-Schiff (PAS) and Masson. Immunohistochemical studies were also performed based on formalin-fixed and paraffin-embedded tissue. The monoclonal antibodies used were against Leu-7, Vimentin, S-100, smooth muscle actin (SMA), Melan-A, human melanoma black-45 (HMB-45), Ki-67, and neuron-specific enolase (NSE). This study was approved by the Institutional Review Board of Beijing Tongren Hospital.

Literature review

A literature search was performed in electronic databases including PubMed, Embase, Web of Science, and Cochrane Library using the following terms: "schwannoma", "intraocular schwannoma", "neurilemmoma", "neurinoma", "uveal schwannoma", "choroidal schwannoma". The publications were limited for human studies and manuscripts written in English. The last search date was July 1st, 2021. All identified full-text references were reviewed by two authors (LD and HYL). After selection, references with relative information and available data were included in the literature review.

Results

The basic characteristics of the included patients were presented in Table 1. A total of 28 patients were histopathologically diagnosed as intraocular schwannoma. The median age (range) of all of the patients was 39 (12–64) years old, among whom half cases were female. Visual loss was the most common symptoms (75.0%), followed by visual field loss (10.7%). Almost all intraocular schwannoma (27/28) presented as nonpigmented mass (Fig. 1), which occurred mainly in ciliary body (42.9%), followed by choroid (32.1%) and ciliochoroid (25.0%). An adjacent retinal detachment was common (Fig. 2). Fundus fluorescein angiography and indocyanine green angiography revealed multiple hyperfluorescent areas in the neoplasma in the early phase followed by its marked staining in the late phase (Fig. 3). In magnetic resonance imaging (MRI), intraocular schwannoma often showed equal signal intensity in T1-weighted images and low signal intensity in T2-weighted images (Fig. 4), while in ultrasonography the tumor usually presented as mushroom mass with relatively medium internal reflectivity (Fig. 5). For tumors located in anterior segment, ultrasonic biological microscopy always revealed a medium internal reflectivity in ciliary body, with iris and lens affected (Fig. 6). 16 patients (57.1%) had history of clinically misdiagnosis as uveal melanoma. Tumor excision was performed for all patients by senior author WBW, and increased light transmission of the tumor was detected in 50.0% cases during the surgery. Consecutive follow-up was conducted for all patients, with the median of 6.0 (0.5–16.0) years. No recurrence or metastasis case was found in any included patients.

Table 1
Characteristics of the included patients.

Number	Year	Sex	Age (year)	Symptom (duration)	Tumor location	Clinical diagnosis	Treatment	Tumor size (mm)	Light transmission
Case 1	2005	M	28	Visual field loss (4 mos)	Ciliochoroid	Uveal melanoma	Excision	18×15×12	Increased
Case 2	2008	F	54	Visual loss (6 yrs)	Choroid	Unknown	Excision	10×8×7	Unknown
Case 3	2009	M	46	Visual loss (5 yrs)	Choroid	Uveal melanoma	Excision	11×8×5	Increased
Case 4	2010	M	22	Visual loss (3 weeks)	Ciliochoroid	Unknown	Excision	Unknown	Increased
Case 5	2010	F	32	Visual loss (3 mos)	Ciliary body	Unknown	Excision	8×6×5	Increased
Case 6	2010	F	49	Visual loss (2 yrs)	Ciliary body	Unknown	Excision	8×6×5	Unknown
Case 7	2011	M	57	Mass (1 mo)	Ciliary body	Uveal melanoma	Excision	9×7×6	Increased
Case 8	2012	F	20	Visual field loss (2 mos)	Ciliochoroid	Uveal melanoma	Excision	15×13×7	Unknown
Case 9	2012	M	34	Visual loss (18 days)	Choroid	Uveal melanoma	Excision	8×7×7	Unknown
Case 10	2014	M	45	Diplopia (2 yrs)	Ciliary body	Unknown	Excision	9×9×5	Unknown
Case 11	2014	M	32	Visual loss (6 mos)	Choroid	Uveal melanoma	Excision	9×8×6	Unknown
Case 12	2015	F	36	Visual loss (2 mos)	Ciliary body	Uveal melanoma	Excision	15×8×7	Increased
Case 13	2015	F	36	Visual loss (1 mo)	Choroid	Uveal melanoma	Excision	10×8×5	Increased
Case 14	2015	F	50	Mass (1 year)	Sclera and ciliochoroid	Uveal melanoma	Excision	16×15×8	Increased
Case 15	2015	M	46	Visual loss (3 mos)	Ciliary body	Uveal melanoma	Excision	13×8×7	Increased
Case 16	2015	F	27	Visual loss (3 mos)	Choroid	Unknown	Excision	12×8×7	Unknown
Case 17	2016	M	32	Visual loss (6 mos)	Ciliary body	Hemangioma	Excision	14×8×7	Unknown
Case 18	2016	F	40	Visual loss (20 days)	Ciliochoroid	Unknown	Excision	13×11×9	Unknown
Case 19	2017	F	46	Visual loss (2 mos)	Ciliary body	Uveal melanoma	Excision	15×11×10	Unknown
Case 20	2017	F	38	Visual field loss (3 mos)	Ciliary body	Hemangioma	Excision	11×8×5	Unknown
Case 21	2017	F	23	Visual loss (2 mos)	Ciliary body	Unknown	Excision	13×7×7	Increased

Number	Year	Sex	Age (year)	Symptom (duration)	Tumor location	Clinical diagnosis	Treatment	Tumor size (mm)	Light transmission
Case 22	2017	F	38	Visual loss (6 mos)	Ciliochoroid	Uveal melanoma	Excision	15×12×10	Increased
Case 23	2018	M	64	Visual loss (3 mos)	Choroid	Uveal melanoma	Excision	10×10×4	Unknown
Case 24	2018	M	45	Visual loss (1 yrs)	Ciliochoroid	Uveal melanoma	Excision	6×5×5	Unknown
Case 25	2018	F	12	Mass (2 mos)	Ciliary body	Uveal melanoma	Excision	19×15×9	Unknown
Case 26	2019	M	47	Visual loss (1 mo)	Choroid	Unknown	Excision	3×3×3	Unknown
Case 27	2019	M	43	Visual loss (1 mo)	Choroid	Uveal melanoma	Excision	7×6×6	Increased
Case 28	2021	M	48	Visual loss (1 mo)	Ciliary body	Unknown	Excision	10×7×5	Unknown

Immunohistochemical studies were performed in 26 cases. Most cases diffusely immunoreacted with antibodies to S-100 protein and Vimentin (Fig. 7). There was no immunoreactivity for muscle marker SMA or melanocytic markers (Melan-A and HMB45). Immunostaining with the proliferation marker Ki-67 labeled less than 1% of the neoplastic nuclei.

The literature search identified 36 references with 49 cases after removal of duplicates [2, 4–38]. A brief summary of the main findings in publications was presented in Table 2. The median age (range) was 33 (0.5–76) years old, and 32 patients (65.3%) were female. Visual loss was the most common symptom (67.3%). The neoplasma occurred mostly in choroid (53.1%), followed by ciliary body (28.6%), and ciliochoroid (18.4%).

Table 2
Summary of reported intraocular schwannoma

Author	Age (year)	Sex	Symptom	Tumor Location	Tumor Size (mm)	Light Transmission	Treatment	Follow-up
Cho [4]	30	F	Elevated IOP	Choroid	30×10×10	N/A	Excision	N/A
Damato [5]	28	F	Visual loss	Ciliochoroid	N/A	N/A	Enucleation	N/A
	37	F	Visual loss	Choroid	6.9×5.8×2.1	N/A	Biopsy	11 years
	33	M	Visual loss	Choroid	7.5×6.9×3.9	N/A	Biopsy	11 years
	45	M	Visual loss	Choroid	18×18×10	N/A	Biopsy	1 year
	15	M	Visual loss	Choroid	12×12×3.6	N/A	Biopsy	6 years
Donovan [6]	68	F	Visual loss	Ciliary body	6×10	Increased	Enucleation	N/A
Fan [7]	21	M	Visual loss	Choroid	13×13×6	Decreased	Enucleation	N/A
Freedman [8]	31	M	Visual loss	Choroid	24×24×23.5	N/A	Enucleation	N/A
Goto [9]	19	F	Mass	Ciliary body	7×7×9	N/A	Excision	4 years
Graham [10]	11	F	Mass	Choroid	19×7×7	Increased	Excision	2 years
Huang [11]	37	F	Visual loss	Choroid	10×9×5	N/A	Excision	1 week
Hufnagel [12]	57	F	Visual field loss	Ciliary body	7.5×9.5	Increased	Excision	15 years
Jajapuram [13]	56	M	Visual loss	Choroid	4.5×4.5×6	N/A	Enucleation	N/A
	33	F	Visual loss	Choroid	10×6	N/A	Enucleation	N/A
John [14]	0.5	F	Intermittent esotropia	Choroid	5×12.5	N/A	Enucleation	N/A
Kalik [15]	58	M	N/A	Choroid	N/A	N/A	Enucleation	15 weeks
Kim [16]	39	F	Visual loss	Ciliary body	17×17×22	N/A	Enucleation	N/A
Kiratli [17]	11	M	Visual loss	Ciliary body	15×15×7	N/A	Enucleation	N/A
Kuchle [18]	26	M	Visual loss	Ciliary body	5×5	N/A	Excision	N/A
Lee [19]	74	F	Visual loss and proptosis	Choroid	10×12.2×12.1	N/A	Enucleation	5 years
Matsuo [20]	73	F	Eye irritation	Choroid	N/A	N/A	Enucleation	N/A
McLaughlin [21]	34	F	Mass	Intrascleral	2	N/A	Autopsy	N/A
Mortuza [22]	58	M	Eye pain	Entire globe	2.3×2×2	N/A	Enucleation	N/A
Nair [23]	12	M	Subconjunctival mass	Entire globe	N/A	N/A	Excision	26 months

F: female, M: male, IOP: intraocular pressure, N/A: not available.

Author	Age (year)	Sex	Symptom	Tumor Location	Tumor Size (mm)	Light Transmission	Treatment	Follow-up
Packard [24]	43	F	Visual loss	Choroid	N/A	N/A	Enucleation	N/A
Pineda [25]	46	M	Mass	Ciliary body	2×1×1	Increased	Enucleation	N/A
Quintana [26]	76	F	Proptosis	Choroid	25×23×22	N/A	Enucleation	N/A
Rosso [27]	40	F	Visual loss	Choroid	15	Increased	Enucleation	N/A
Saavedra [28]	9	F	Mass and visual loss	Iris and ciliochoroid	6×3	N/A	Enucleation	7 years
Shields [29]	70	F	Mass	Choroid	9×9×3	Decreased	Excision	6 months
Shields [30]	14	F	Visual loss	Choroid	14×3	Decreased	Enucleation	N/A
Shields [31]	30	M	Ptosis	Choroid	7×6×3.5	N/A	Enucleation	N/A
Smith [32]	30	F	Visual loss	Choroid	15×11×15	Increased	Enucleation	N/A
Swan [33]	32	F	Visual loss	Choroid	Cherry	N/A	Enucleation	N/A
Thaller [34]	28	F	Visual loss	Ciliary body	N/A	Increased	Enucleation	N/A
Turell [35]	47	M	Visual loss	Ciliochoroid	17×15×11.4	Decreased	Excision	N/A
Udyaver [36]	19	M	Episcleral mass	Ciliary body	13×13×11.5	Increased	Biopsy	4 months
Xian [37]	63	F	Visual loss	Ciliary body	8×6×6	N/A	Excision	N/A
	38	F	Visual loss	Ciliochoroid	10×10×10	N/A	Excision	N/A
	36	F	Visual loss	Choroid	13×10×9	N/A	Enucleation	N/A
	22	F	Visual loss	Ciliochoroid	16×13×11	N/A	Excision	N/A
	19	F	Visual loss	Ciliochoroid	15×13×12	N/A	Excision	N/A
	37	F	Visual loss	Ciliochoroid	27×15×12	N/A	Excision	N/A
You [2]	23	F	Visual loss	Choroid	12.6×15.5	Increased	Enucleation	11 months
Yu [38]	25	M	Visual loss	Ciliochoroid	10.1×8.8	N/A	Excision	N/A
	48	F	Visual loss	Ciliary body	16.7×11.2	N/A	Excision	3 months
	30	M	Visual loss	Ciliary body	N/A	N/A	Excision	16 months
	18	F	Visual loss	Iris	N/A	N/A	Excision	6 months
F: female, M: male, IOP: intraocular pressure, N/A: not available.								

Discussion

Intraocular schwannoma is a rare and benign peripheral nerve neoplasma that usually appears as solitary and amelanotic lesion in the ciliary body or choroid. So far, a total of 49 cases of intraocular schwannoma have been reported, and we have collected another 28 cases, which contains the largest sample size in a single center. Among all these 77 cases, intraocular

schwannoma occurs more often in female than male with a ratio of 2:1. This trend is also consistent with schwannomas that occur in other parts of human bodies [39].

In our study, choroidal schwannoma was often clinically misdiagnosed as amelanotic melanoma, because of the similar shape and color. Even MRI and ultrasonography cannot provide distinguished characteristics exactly. However, we still considered they were more likely to be benign tumors such as schwannoma, neurofibromatosis, or hemangioma. Therefore, we chose to excise the mass with vitrectomy, and the histopathologic findings confirmed our speculation.

Considering with the experience of previously reported cases, it is very difficult to differentiate intraocular schwannoma with amelanotic melanoma, hemangioma, and metastatic carcinoma. Clinical features, ultrasonography, and MRI findings in schwannoma can only provide limited clues to identify those tumors. It is often impossible to make a definite diagnosis before histopathologic examination, which makes it difficult to choose treatment strategies. Surgical excision or tissue biopsy may be a better choice when diagnosing an amelanotic neoplasma. For those cases with huge intraocular mass and severe vision loss, enucleation can also be considered. Immunohistochemistry based on histopathological slide is helpful in the diagnosis of intraocular schwannoma, especially in differentiating with uveal melanoma and neurofibroma. Schwannoma diffusely immunoreacts with antibodies to S-100 protein and frequently expresses Vimentin and Leu-7 [40].

Generally, the prognosis of intraocular schwannoma is favorable. Malignant change of schwannoma is rare, so that it has not been reported in any intraocular location. Only one case was reported with recurrence after local excision [12].

In conclusion, intraocular schwannoma is a rare and benign tumor, which is often misdiagnosed as uveal melanoma. Therefore, cautions should be taken when diagnosing an amelanotic intraocular mass.

Conclusion

Intraocular schwannoma is a rare benign intraocular tumor. It usually presents as nonpigmented mass, which is easily misdiagnosed as nonpigmented uveal melanoma.

Abbreviations

PAS: periodic acid-Shiff, SMA: smooth muscle actin, HMB-45: human melanoma black-45, NSE: neuron-specific enolase, Melan-A and HMB45: melanocytic markers.

Declarations

Ethics approval and consent to participants

Ethics approval and informed consent were not required for this study because of public accessibility to the data.

Consent for publication

Not applicable.

Availability of data

Not applicable.

Competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

This study was supported by The Capital Health Research and Development of Special (2020-1-2052), Science & Technology Project of Beijing Municipal Science & Technology Commission (Z201100005520045, Z181100001818003), the Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20150201).

Authors' contributions

W.B. Wei, Y.M Li and L. Dong designed the study, Y.M Li, L. Dong and X.L Xu wrote the manuscript. H.Y Li, Q.Yang, and R.H Zhang collected the data and conducted the analyses, W.B. Wei edited and revised the manuscript. All authors have approved the submitted version and agreed with the contributions declarations.

Acknowledgements

Not applicable.

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Figures

Figure 1

Appearance of intraocular schwannoma of Case 10 (A), Case 20 (B), and Case 25 (C) that located in ciliary body. Blue arrow: tumor.

Figure 2

Ultra-widefield fundus image of intraocular schwannoma of Case 24, and an adjacent retinal detachment was also noted.

Figure 3

Fundus fluorescein angiography (A) and indocyanine green choroidal angiography (B) of Case 24.

Figure 4

Magnetic resonance imaging (MRI) showed equal signal intensity in T1-weighted images and low signal intensity in T2-weighted images of intraocular schwannoma of Case 27.

Figure 5

Ultrasonography showed a mushroom mass with relatively medium internal reflectivity of Case 21.

Figure 6

Ultrasonic biological microscopy of case 28 revealed a medium internal reflectivity in ciliary body, with iris and lens affected.

Figure 7

Hematoxylin-eosin-stained slide (A) with immunohistochemical examination of S-100 (B) and Vimentin (C) of Case 28.