

Multimode imaging characteristics and treatment of uveal schwannoma

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Abstract

• **AIM:** To delineate the different imaging characteristics of uveal schwannoma from melanoma and discuss the optimal treatment strategy for intraocular schwannoma.

• **METHODS:** Case series of three patients diagnosed with intraocular schwannoma was collected at Zhongshan Ophthalmic Center, Guangzhou, China from July 2014 to December 2020. All the study patients underwent ultrasonography and magnetic resonance imaging (MRI). The clinical features, therapeutic strategies, and prognoses of all patients were reviewed.

• **RESULTS:** Ultrasonography of all three patients (all females, mean age, 39y, age range, 23-54y) showed low to medium reflectivity with a homogeneous internal structure. MRI of all three patients demonstrated isointensity on T1-weighted imaging spin-echo (T1WI SE) images and hypointense on fast spin-echo T2-weighted images (FSE T2WI) images with respect to the brain. Minimally invasive pars plana vitrectomy (PPV) and local resection of the tumor was performed for all patients, and the diagnosis of schwannoma was confirmed by histopathological examination.

• **CONCLUSION:** The present study indicates that ultrasonography and MRI features of uveal schwannoma may contribute to the differentiation of uveal schwannoma from melanoma, and the optimal therapy for intraocular schwannoma is minimally invasive PPV and local resection.

• **KEYWORDS:** uveal schwannoma; ultrasonography; magnetic resonance imaging; imaging characteristics; pars plana vitrectomy

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INTRODUCTION

Schwannoma is a slow-growing solitary benign tumor originating from Schwann cells of the peripheral nerve sheath^[1]. The benign uveal tumor can exhibit extrascleral extension, mimicking inflammatory and malignancy processes, which preferentially involves the head, neck, and extremities^[2-4]. Intraocular schwannoma, presumed to originate from the ciliary nerve in the uvea, is rare, with only 50 reported cases in the literature^[5]. Intraocular schwannomas are presumed to arise from ciliary nerves in the uvea, and most of our current knowledge came from limited case reports or case series involving the iris, ciliary body, and choroid^[6]. This type of tumor rarely undergoes malignant transformation and is nonlethal, however, due to the difficulty of diagnosis, many patients can only be diagnosed through histopathological sections after the extraction^[7-9]. Therefore, appropriate diagnosis and treatment are required to avoid vision loss or even blindness from severe retinal detachment or tumor growth.

A uveal tumor is usually diagnosed preoperatively by ophthalmoscopy, ultrasonography, and magnetic resonance imaging (MRI) examinations^[1,10]. However, uveal schwannoma is often misdiagnosed as malignant melanoma, leading to unnecessary enucleation in clinical practice^[11]. In a previous review of intraocular schwannoma, 44% of eyes were enucleated due to a high suspicion of malignant melanoma^[12].

Therefore, presurgical differentiated diagnosis between uveal schwannoma and melanoma based on clinical presentation and examinations is challenging but of crucial importance.

In the present study, we reviewed three patients with intraocular schwannoma who have been treated with pars plana vitrectomy (PPV) and local tumor resection, to discuss how to differentiate uveal schwannoma from melanoma based on multi-mode imaging examinations, as well as the optimal surgical plan to retain the crystal lens and eyeball.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the Institutional Review Board of Zhongshan Ophthalmic Centre (ZOC), Affiliated with Sun Yat-sen University, Guangzhou, China, and performed in accordance with the World Medical Association's Declaration of Helsinki. Informed consent was obtained from all of the patients.

A consecutive interventional case series of three eyes of three female patients seen at ZOC of Sun Yat-sen University from July 2014 to December 2020 with schwannoma is reported. The diagnosis was based on detailed ophthalmic examination, B-scan ultrasonography, fluorescein fundus angiography (FFA), indocyanine green angiography (ICGA), spectral-domain optical coherence tomography (SD-OCT), and MRI. All eyes received small-gauge PPV (Constellation Vitrectomy System, Alcon Laboratories Fort Worth, TX, USA) by the same experienced ophthalmologist (Zhang SC) with retrobulbar anaesthesia under monitored anaesthesia care. Silicone-oil injection were also performed. Tumors were examined by light microscopy and immunohistochemical studies.

RESULTS

Case 1 A 39-year-old woman presented to our hospital with a 2-year history of decreasing visual acuity (VA) in her oculus dexter (OD). She denied any systemic disease. The best corrected VA was hand motion, and the intraocular pressure (IOP) was 19 mm Hg. Her anterior segment examination was unremarkable. Ophthalmic examination of the OD was also normal. Ophthalmoscopic examination demonstrated a large posterior retinal detachment overlying an amelanotic mass (7 to 8 times the papillary diameter) in her OD (Figure 1A). On ultrasonography, the mass has a homogeneous internal structure and exhibits relatively low to moderate reflectivity, measuring 12.8 mm wide and 8.1 mm high (Figure 1B). SD-OCT confirmed a subretinal hyper-reflective mass, supratemporal to the fovea, with underlying hypo reflectivity corresponding to the mass (Figure 1C). FFA showed a big uveal space-occupying lesion with hypo-fluorescence at the superior temporal margin of the optic disc. Progressive choroidal hyper-fluorescence small-caliber vessels were seen in the initial phase without retinal-choroidal anastomosis, and staining of the tumor and fluorescein leakage were observed in

the late phase (Figure 1D). ICGA also revealed the choroidal mass, intrinsic choroidal vasculature (double circulation) in the early phase, and in the late phase massive fluorescein leakage was also observed (Figure 1E). MRI showed uveal schwannoma hyperintense on T1-weighted imaging spin-echo (T1WI SE) images and hypointense on fast spin-echo (FSE) T2-weighted images (T2WI) images in this patient and in the other two patients as well, with respect to the vitreous body. However, uveal schwannoma showed isointensity on T1WI SE and FSE T2WI images with respect to the brain (Figure 1F).

Diagnostic possibilities included an amelanotic melanoma and neuro-derived neoplasm. Because the consensus among several ophthalmologists and radiologists was that the tumor was more likely to be benign, a 25 gauge PPV with tumor resection under general hypotension anesthesia was performed. First remove the posterior and peripheral vitreous. Barrier endolaser photocoagulation and electrocoagulation were done around the retinal and choroidal defect. Separate the choroid around the tumor, and then the tumor was completely excised. Silicone oil tamponade was performed after fluid/air exchange. The main theoretical advantages of silicone oil over gas are its lack of absorption and persistence, which allows long-term, sustained, and direct tamponade to the retina^[13-17]. When preretinal membranes re-proliferation and proliferative vitreoretinopathy or persistent/retinal neovascularization occur in the postoperative period, in theory silicone oil's persistent tamponading effect on the retina might support the retina better to decrease the rate of vitreous hemorrhage to a greater extent or reduce the incidence of retinal detachment than a fluid-filled vitreous cavity after gas reabsorption. Finally, the excised tumor was sent for light microscopy and immunohistochemical study. One week after the surgery, the VA of the patient was counting fingers OD. The retina was flat, and limited hemorrhage was observed in the area of the retina and choroid defect. Hematoxylin and eosin staining (HE) demonstrated that the tumor was composed of spindle-shaped cells which were densely arranged in bundles with abundant cytoplasm and round nucleus (Figure 1G). Immunohistochemical evaluation results were as follows: S-100(+), GFAP(+), SMA(-), Vimentin(+), NF(-), Sy(-) and Ki-67(5%+). No melanosomes were recognized in the neoplastic cells. Therefore, the confirmed diagnosis of choroidal schwannoma was made in the OD. Six months later, the lens was transparent, and the silicone oil was removed. Her VA improved to 4/200 at the 20-month follow-up, and IOP was 15 mm Hg.

Case 2 A 23-year-old young Chinese woman complained about VA deterioration over 4mo in her OD. She was otherwise healthy, and no family or ocular injury history was declared. The left eye was unremarkable. Her VA was hand motion OD. IOP in both eyes were within normal limits at

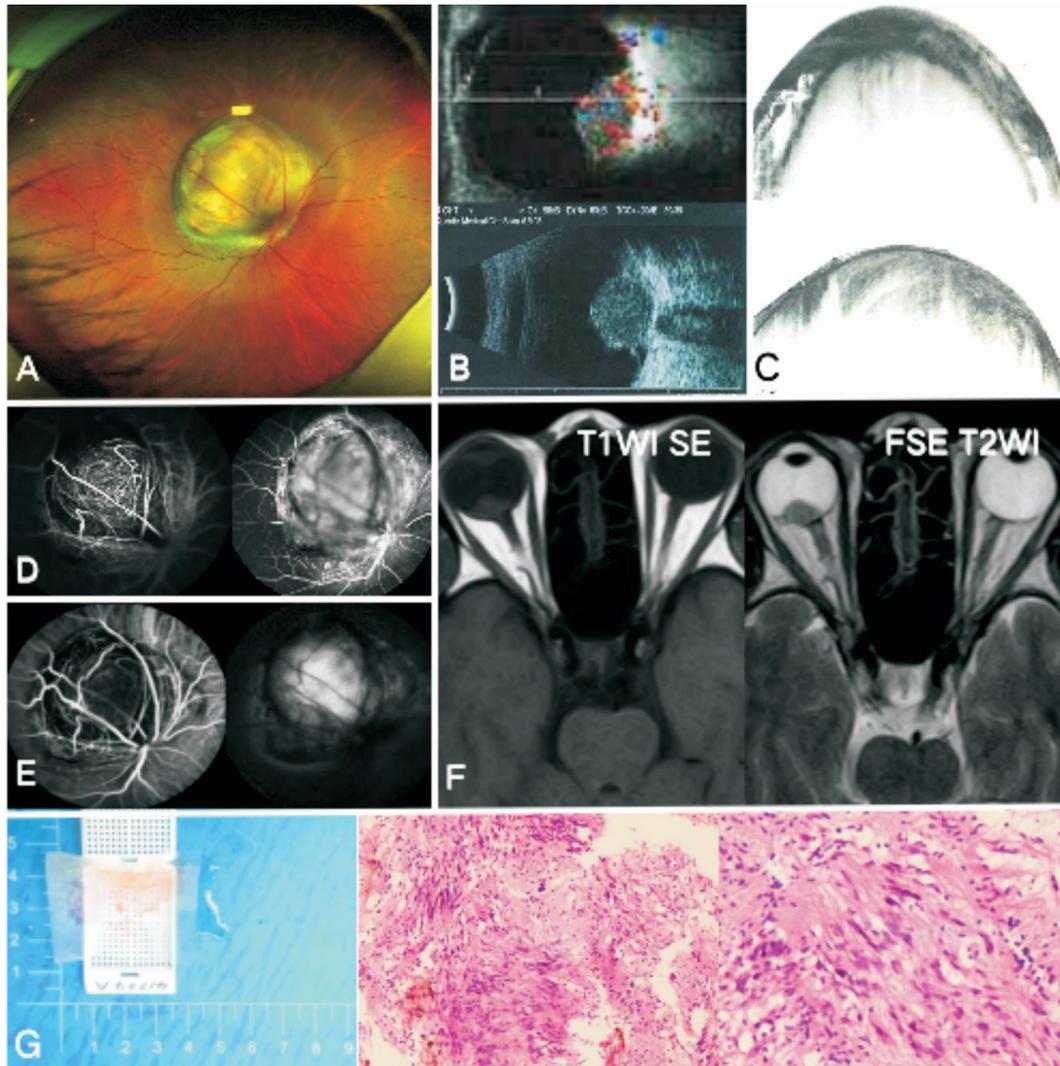


Figure 1 The ophthalmoscopic examination, ultrasonography, SD-OCT, fluorescein angiography, indocyanine green angiography, MRI and hematoxylin and eosin (HE) staining of Case 1 A: Ophthalmoscopy demonstrated a large posterior retinal detachment overlying an amelanotic mass (7 to 8 times the papillary diameter) in her right eye. B: On ultrasonography, the mass showed relatively low to medium reflectivity with a homogeneous internal structure and was measured 12.8 mm in width and 8.1 mm in height. C: SD-OCT showed a hyperreflective band associated with intra-subretinal fluid and hairy photoreceptors. D: Fluorescein angiography (FFA) showed a big uveal space occupying lesion with hypo-fluorescence at the superior temporal margin of the optic disc. Progressive choroidal hyper-fluorescence small-caliber vessels were seen in the initial phase without retinal-choroidal anastomosis and staining of the tumor and fluorescein leakage were observed in the late phase. E: Indocyanine green angiography (ICGA) also revealed the choroidal mass, intrinsic choroidal vasculature (double circulation) in the early phase and massive fluorescein leakage in the late phase were also observed. F: MRI showed that uveal schwannoma was hyperintense on T1WI spin-echo (SE) images and hypointense on fast SE (FSE) T2-weighted images (T2WI) with respect to the vitreous body in all 3 patients. Nevertheless, uveal schwannoma showed isointensity on T1WI SE and FSE T2WI images with respect to the brain. G: HE staining demonstrated that the tumor was composed of spindle-shaped cells which were densely arranged in bundles with abundant cytoplasm and round nucleus.

17 mm Hg. The anterior segment in the OD was normal. Ophthalmoscopy demonstrated a large inferotemporal serous retinal detachment overlying an amelanotic mass (Figure 2A). On ultrasonography, the tumor was measured 15.6 mm in width and 12.1 mm in height, and the mass showed medium internal reflectivity (Figure 2B). Ultrasound biomicroscope revealed a giant mass on the inferotemporal quadrant of the ciliary body. The anterior region's acoustic reflectivity was

of low-to-middle grade (Figure 2C). FFA showed significant protrusion of the retinal and ciliary body into the vitreous in the inferior temporal quadrant as well as a hypo-fluorescence choroidal mass, which was also revealed on indocyanine green angiography. MRI revealed a choroidal mass with intermediate T1- and T2-signal intensity, which showed homogenous contrast enhancement with respect to the brain (Figure 2D).

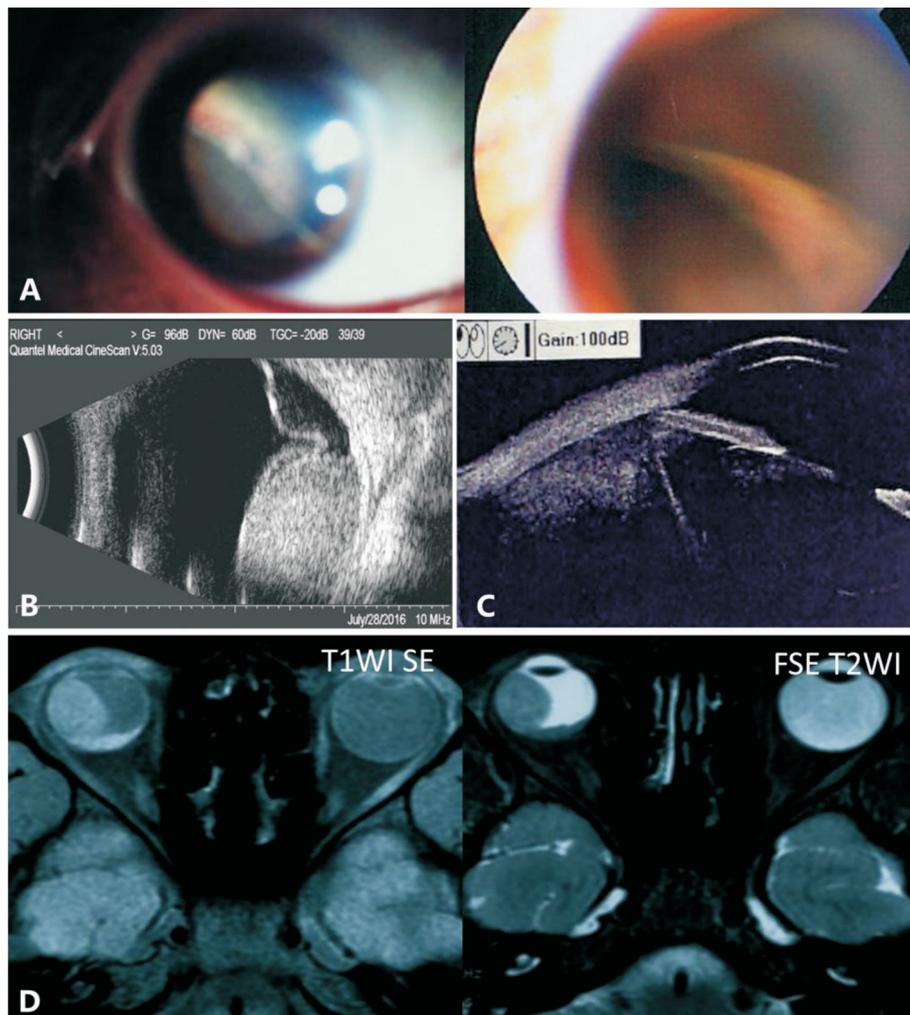


Figure 2 The ophthalmoscopic examination, ultrasonography, SD-OCT, FFA, ICGA and MRI of Case 2 A: Ophthalmoscopy demonstrated a large inferotemporal serous retinal detachment overlying an amelanotic mass; B: On ultrasonography, the tumor was measured 15.6 mm in width and 12.1 mm in height, and the mass showed medium internal reflectivity; C: Ultrasound biomicroscope showed a giant mass on the inferotemporal quadrant of the ciliary body; The anterior region's acoustic reflectivity was of low-to-middle grade. D: MRI demonstrated a choroidal mass with intermediate T1- and T2-signal intensity, which showed homogenous contrast enhancement with respect to the brain.

Following a thorough medical examination, the patient was given a initially diagnosis of the choroid and ciliary body mass with the exudative retinal detachment of the OD. Under general hypotension anesthesia, a trans-scleral local excision, 23 gauge PPV, and silicone-oil tamponade were performed, and the tumor was completely resected and sent for histopathological examination. Histopathology examination identified that the tumor was composed of spindle cells with mild cytoplasm and well-differentiated. The majority of spindle cells were arranged in bundles and some areas in a palisading pattern. Besides, the immunohistochemical evaluation showed that the tumor was positive for S-100, CD34, SMA, Vimentin, and Ki-67, which confirmed the diagnosis of schwannoma. Therefore, the pathological diagnosis was a schwannoma of the choroidal and ciliary body in the OD. No complications occurred during the peri- or post-operative courses. Three months after the surgery, the patient's VA was hand motion with an IOP of 14 mm Hg

in the OD, and the lens was transparent. Examination of the fundus showed that the retina was reattached.

Case 3 A 54-year-old healthy Chinese woman reported that a tumor was found in her OD during a physical examination half a month ago. No reduction or dysfunction of vision was reported in either eye. She denied any systemic disease. Ophthalmic examination of her left eye was normal. Her best corrected VA was 1.0 and the IOP was 16.3 mm Hg in the OD. A large, nonpigmented choroidal mass was observed from the superior temporal fundus of her OD, with large tortuous retinal vessels on the surface (Figure 3A). The mass showed low to medium internal reflectivity with a homogeneous internal structure and was 8.1 mm in width and 4.4 mm in height on ultrasonography (Figure 3B). FFA and ICGA findings were similar to Case 1 (Figure 3C, 3D). MRI revealed a choroidal mass with intermediate T1- and T2-signal intensity with homogenous contrast enhancement with respect to the brain.

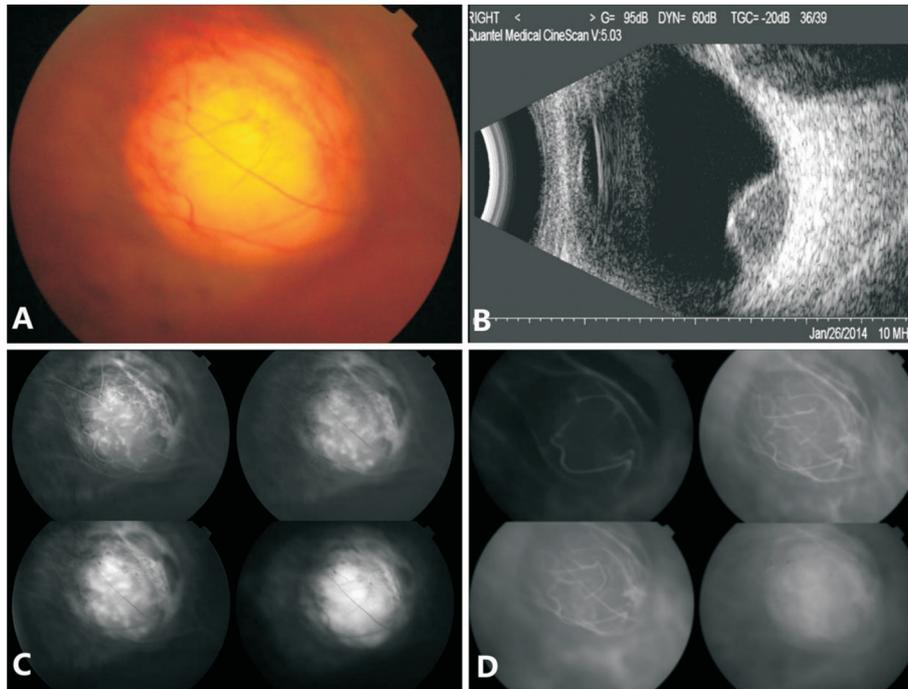


Figure 3 The ophthalmoscopic examination, ultrasonography, fluorescein angiography and indocyanine green angiography of Case 3 A: A large, nonpigmented choroidal mass was observed from the superior temporal fundus of her right eye, with large tortuous retinal vessels on the surface. B: The mass showed low to medium internal reflectivity with a homogeneous internal structure and was 8.1 mm in width and 4.4 mm in height on ultrasonography. C: FFA showed a big uveal space occupying lesion with hypo-fluorescence at the superior temporal margin of the optic disc, progressive choroidal hyper-fluorescence small-caliber vessels were seen in the initial phase without retinal-choroidal anastomosis, following by staining of the tumor and fluorescein leakage in the late phase. D: ICGA showed the choroidal mass, intrinsic choroidal vasculature (double circulation) in the early phase and massive fluorescein leakage in the late phase were also observed.

Following a complete medical examination, the preliminary diagnosis by several ophthalmologists and radiologists was a benign uveal tumor, with a high likelihood of intraocular schwannoma. Thus, choroidal mass excision through 27 gauge PPV with silicone oil tamponade was performed. HE staining revealed that the tumor was composed of spindle-shaped cells which were densely arranged in bundles with abundant cytoplasm and oval nucleus. Immunohistochemistry examination results of the tumor specimen were as follows: S-100(+), GFAP(+), SMA(-), Vimentin(+), and Ki-67(<1%+). Thus, the confirmed diagnosis of choroidal schwannoma was made in the OD. The patient was followed up for 4mo and remained tumor-free, her best corrected VA increased to 20/30 with an IOP of 16 mm Hg at 4mo postoperatively.

DISCUSSION

Intraocular schwannoma is a rare benign peripheral nerve neoplasm that usually presents as a solitary amelanotic lesion of the uvea^[3,12]. The tumor most commonly arises from the choroid and ciliary body, and the iris is less frequently involved. Most reported patients were adult females and malignant change has not been reported by far^[11].

Given that often masquerades the amelanotic choroidal melanoma, the majority of previously reported cases were diagnosed after enucleation^[3,18]. The survival of amelanotic

melanoma is poorer than due to more advanced stage at diagnosis^[19-20]. In the prior reports, this disease was more common in white people, there was no significant gender difference in gender and the lesions presented with based ≥ 8 mm frequently^[21-22]. Most lesions of amelanotic choroidal melanoma are associated with subretinal fluid (60%) and most are dense on ultrasound (54%), the mean distance to foveola is closer. The amelanotic choroidal melanoma do not demonstrate hyperintense signal on T1-weighted MRI and hypointense signal on T2-weighter images liked melanoma usually^[23-27]. The limited knowledge of intraocular schwannoma makes it challenging to differentiate from melanoma before the operation, although clinical features, ultrasonography, FFA, ICGA, and MRI findings can provide some clues. In the present case series, we found that ophthalmic ultrasound and MRI imaging may be helpful when trying to differentiate between uveal schwannoma and melanoma. B-scan of our patients showed low to medium reflectivity with a homogeneous internal structure. The lack of choroidal excavation and orbital shadowing on ultrasonography argued against a melanoma, which is consistent with the previous literature^[28]. More importantly, MRI showed that uveal schwannoma was hyperintense on T1WI SE images and hypointense on FSE T2WI in all three

patients with respect to the vitreous body. Nevertheless, uveal schwannoma demonstrated isointensity on T1WI SE and FSE T2WI images in all three patients with respect to the brain. On postcontrast T1WI images, all three patients showed markedly homogeneous enhancement, consistent with previous studies^[29-30]. Unlike uveal schwannoma, with respect to the brain, uveal melanoma still demonstrated hyperintensity on SE T1WI and hypointensity on FSE T2WI. Therefore, the difference in ultrasound characteristics and signal intensity of the tumor with respect to the brain on MRI images may be used to differentiate uveal schwannoma from melanoma.

Though benign in nature, most reported cases of intraocular schwannoma underwent enucleation because of the possibility of malignant melanoma^[3,5]. Previous studies had also suggested surgical excision of the tumor followed by immunohistochemistry analysis for cases suspicious for intraocular schwannoma and with a low likelihood of malignancy, but to the best of our knowledge, only five such cases had been reported^[11,18,30]. Local resection can preserve a viable globe and are potentially sight-saving, thus reliable non-invasive examination is of great importance for differential diagnosis, as well as to guide subsequent treatment and reduce the enucleation rate. In all our three cases, the presurgical clinical diagnosis of uveal schwannoma was made based on the multimode imaging examinations, especially MRI and ultrasonography, and was confirmed by immunohistochemistry examination after the surgery. We applied the treatment strategy of choroidal mass excision through minimally invasive PPV, which can not only successfully retain a viable globe and even a transparent lens but also preserve the VA and normal IOP. Another advantage of this treatment strategy was the excision of a giant intraocular tumor through a minimal surgical wound and therefore the cosmetic outcome was more desirable. No complications were observed, and all three patients were subjectively doing well during the follow-up.

In conclusion, the present study indicates that ultrasonography and MRI features of uveal schwannoma may contribute to presurgical differentiation of uveal schwannoma from malignant uveal lesions, and minimally invasive PPV with local resection could serve as the optimal therapy for intraocular schwannoma.

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Authors' contributions: Zhang T collected the data of the patients, Feng LJ analysed the data of the patients, Wang Y wrote the manuscript, Wang Y and Wei YT collected the pictures of ultrasonography and MRI of the patients, Shi YH,

Wang L, and Sun YM revised the manuscript, Zhang SC supervised the project and reviewed the paper. All authors have read and approved the published version of the manuscript.

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