

Intraocular schwannoma: A case series of 3 patients

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Abstract. Schwannoma is a proliferation of neoplastic Schwann cells. Schwannomas comprise 8-10% of all primary intracranial tumors. Primary intraorbital schwannoma arising from the ciliary nerves in the uvea, which accounts for 1-2% of all intracranial tumors, is a rare intraocular neoplasm. Intraocular schwannoma frequently masquerades as melanoma, reflecting the difficulty in clinically distinguishing it from malignant melanoma and the requirement for a histopathological diagnosis. The aim of the present study was to report a case series of 3 patients diagnosed with intraocular schwannoma at the Department of Ophthalmology, Peking University People's Hospital (Beijing, China). Patients with intraocular schwannoma were identified by searching the computerized database and patient medical records of the Department of Ophthalmology of Peking University People's Hospital. The patients (2 men and 1 woman; mean age, 34 years; age range, 25-48 years) were all treated by trans-scleral local resection, and schwannoma was confirmed by biopsy. The study found that choroidal schwannoma has a variety of clinical manifestations, with iridodialysis, subluxation of the lens and exudative detachment of the retina observed. The present study indicates that a pathological biopsy is required for diagnosis and that the optimal therapy is local resection.

Introduction

Schwannomas (neuroma, neurinoma or neurilemmoma) are benign encapsulated peripheral nerve sheath neoplasms that arise from Schwann cells, which produce myelin. Approximately 8% of head and neck schwannomas involve the intracranial portion of a peripheral nerve sheath (1,2). Primary intraorbital schwannomas account for only 1-2% of all

intracranial tumors (3). Intraocular schwannomas arise from ciliary nerves in the uvea, mostly in the ciliary body or choroid and occasionally in the iris (4-7). Intraocular schwannomas are benign encapsulated tumors consisting of a pure proliferation of Schwann cells and are not life threatening; however, they can cause impairment and blindness via tumor growth and serous retinal detachment, and appropriate treatment is required to prevent vision loss and progressive enlargement of the condition (8-10). Uveal schwannoma is also termed a 'pseudomelanoma', as it simulates the most common type of primary intraocular tumor, uveal melanoma; this term reflects the difficulty in clinically distinguishing the schwannoma from uveal malignant melanoma (11-13). In certain previously reported cases, eyeball enucleation was performed due to a diagnosis of malignant melanoma, and only after subsequent histopathological examination of the surgical specimen was a benign tumor revealed (14-18). In the present study, the cases of 3 patients with intraocular schwannoma who underwent surgical excision locally, retained the eyeball or even achieved an improvement in visual acuity are reviewed.

Case reports

Case 1. A 25-year-old man complained of vision loss that had persisted for 1 month on January 19 2012 at Peking University People's Hospital (Beijing, China). Poor eyesight of the right eye with ametropia had been present since early age. Other past medical and family histories were unremarkable. The best corrected visual acuity was 20/640, with nystagmus, and the intraocular pressure (IOP) was 9 mmHg in the right eye. Slit-lamp biomicroscopy showed a normal anterior segment. Examination of the retina showed a superotemporal, pre-equatorial, pigmentary choroidal tumor in the right eye, which was associated with exudative retinal detachment (Fig. 1). The left eye displayed ametropia and nystagmus, and was otherwise normal. On ultrasonography, the tumor measured 10.1 mm in width and 8.8 mm in height, and the ciliary body was involved (Fig. 1).

Following a complete medical examination, the patient was given a preliminary diagnosis of choroid and ciliary body melanoma with exudative retinal detachment of the right eye. Under general hypotension anesthesia, a trans-scleral local resection was performed, with brachytherapy using a ¹⁰⁶Ru ophthalmic applicator (model CCB) for 19 h. The excised tumor was sent for histopathological examination. Specimens

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was fixed with 4% neutral formalin at 25°C for 6 h and then embedded in paraffin. Hematoxylin and eosin-stained sections (4 μ m) were obtained for light microscopy analysis. Sections (3 μ m) were cut and placed on silanized slides and pretreated at the temperature of 25°C for 15 min in citrate buffer prior to immunostaining in order to improve the staining pattern. Sections were also pre-treated at 25°C for 10 min in 3% hydrogen peroxide blocking reagent for blocking endogenous peroxidase activity. Tissue sections were stained using the following monoclonal primary antibodies (OriGene Technologies, Inc., Beijing, China): Mouse anti-S-100 protein (cat. no. ZM-0224), rabbit anti-Desmin (cat. no. ZA-0610), mouse anti-smooth muscle actin (cat. no. ZM-0003), mouse anti-cluster of differentiation 34 (cat. no. ZM-0046) and rabbit anti-vimentin (cat. no. ZA-0511). The incubation with these antibodies was performed at 37°C for 1 h. The secondary antibody used was horseradish peroxidase-labelled goat anti-mouse/rabbit IgG polymer (cat. no. PV-8000; OriGene Technologies, Inc.). The incubation was performed at 37°C for 30 min. The immunoreaction was visualized by demonstration of conjugated peroxidase with 3,3'-Diaminobenzidine (DAB; cat. no. ZLI-9019; dilution, 1:20; OriGene Technologies, Inc.) as the substrate. The incubation was performed for 5 min at 25°C. The slides were counterstained with hematoxylin following staining with DAB in preparation for light microscopy. The tissue sections were observed 40, 100 and x200 magnification. HE staining revealed a tumor composed of spindle cells that were arranged in bundle. Spindle cells were well-differentiated and mild nuclear pleomorphism was present. Mitotic figures were rare. A palisading arrangement could be observed (Fig. 1). Immunohistochemistry results were as follows: S-100(+), Desmin(-), smooth muscle actin(-), cluster of differentiation 34(-) and Vimentin(+). The confirmed diagnosis of ciliochoroidal schwannoma was therefore made in the right eye upon histopathological examination following the trans-scleral incisional tumor biopsy.

No complications occurred during the operative or post-operative courses. On day 9 post-surgery, the patient's visual acuity was 20/800, with an IOP of 9 mmHg. Examination of Fundus demonstrated that the retina had been reattached. However, the patient did not come back for a follow-up check following discharge from hospital.

Case 2. A 48-year-old otherwise healthy woman presented reporting observations of black shadow flies in the left eye for 5 years and vision loss that had persisted for 1 month on July 9 2014 at Peking University People's Hospital. Past medical and family histories were unremarkable. Ophthalmic examination of the right eye was normal. Visual acuity was 20/50 and the IOP was 13 mmHg in the left eye. A slit-lamp biomicroscopic ophthalmic examination revealed a large, prominent, pink, solid lesion that was rich in blood vessels in the anterior chamber prior to the ciliary body from the 6 to 9 o'clock positions, with iridodialysis and pupillary deformation and shift (Fig. 2). The fundus of the left eye showed multiple yellow mobile vitreous particles that indicated asteroid hyalosis. Examination of the retina showed a nasal choroidal tumor without hemorrhage and exudation (Fig. 2).

Ultrasonography demonstrated asteroid hyalosis in the vitreous humor and an inferior nasal lateral hypoechoic

mass, measuring 16.7 mm in cross-sectional basal diameters and 11.2 mm at its greatest apical height (Fig. 2). Ultrasound biomicroscopy demonstrated a giant mass on the inferior nasal quadrant of the ciliary body. The acoustic reflectivity of the anterior region was of low-to-middle grade (Fig. 2).

A trans-scleral local resection was performed, and the tumor was completely removed and sent for histopathological examination, which was performed according to the aforementioned protocol. Histopathology examination revealed that the tumor was composed of spindle cells, which were bland and well differentiated. In addition, the majority of spindle cells were arranged in bundles and some areas in a palisade pattern, which confirmed the diagnosis of ciliochoroidal schwannoma. However, the patient experienced suprachoroidal hemorrhage during surgery, and was left with only the ability to perceive light. At the final follow-up performed on the patient three months post-surgery, the patient developed retinal detachment without light sensation, the Ciliochoroidal schwannoma was totally removed and the eyeball was preserved.

Case 3. A 30-year-old otherwise healthy man reported loss of visual acuity in the left eye following a injury following a fit 3 months previously on April 26 2013 at Peking University People's Hospital. Past medical and family histories were unremarkable. The ophthalmic examination of the right eye was normal. The patient's best corrected visual acuity (BCVA) was 20/200 and the IOP was 11 mmHg in the left eye. A dilated ophthalmic examination revealed a highly prominent brown, avascular, solid, homogenous lesion in the ciliary body from the 6 to 9 o'clock position, with subluxation of the lens temporally and superiorly (Fig. 3). Examination of the optic disk and retina indicated normal results.

Ultrasound biomicroscopy demonstrated a giant mass behind the inferior nasal quadrant of the iris. The acoustic reflectivity of the anterior region was of medium-to-high grade, with posterior attenuation. A computed tomography scan revealed an area with slightly high density in the antero-inferior vitreous. Magnetic resonance imaging (MRI) demonstrated a lesion as an isointense area on T1-weighted imaging (T1WI), which showed homogenous contrast enhancement, and as an isointense area or an area with slightly high intensity on T2WI (Fig. 3). No other clinically evident tumors were present.

Following a complete medical examination, the patient was given a preliminary diagnosis of a ciliary body tumor with a secondary subluxated lens of the left eye. Under general hypotension anesthesia, the tumor was carefully dissected free and completely removed under a lamellar scleral flap, combined with brachytherapy using the ¹⁰⁶Ru ophthalmic applicator (model CCA) for 24 h. Specimens were sent for histopathological examination, which was performed according to the aforementioned protocol. Histopathology examination revealed that the tumor was composed of spindle cells, which were bland and well differentiated. In addition, the majority of spindle cells were arranged in bundles and some areas in a palisade pattern, which confirmed the diagnosis of schwannoma. Thus, the pathological diagnosis was a schwannoma of the ciliary body in the left eye.

No complications were noted during the operative or postoperative courses. Slit-lamp images captured on

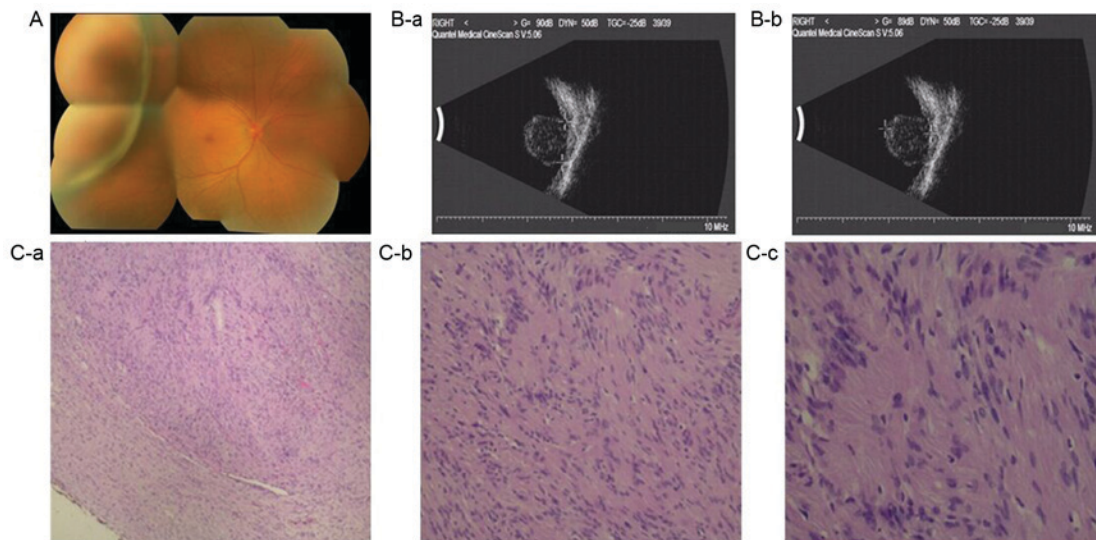


Figure 1. (A) Fundus imaging revealed a superotemporal, pre-equatorial, pigmented choroidal tumor with exudative retinal detachment in the right eye. (B-a and B-b) Ultrasonography revealed a 10.1-mm wide and 8.8-mm high mass involved with the ciliary body. The cross marks on figure B-a represent the width of the mass, and the marks on figure B-b represent the height of the mass. (C) Hematoxylin and eosin staining revealed a tumor composed of spindle neoplastic schwannoma cells that were arranged in bundles, at (C-a) x40, (C-b) x100 and (C-c) x200 magnification.

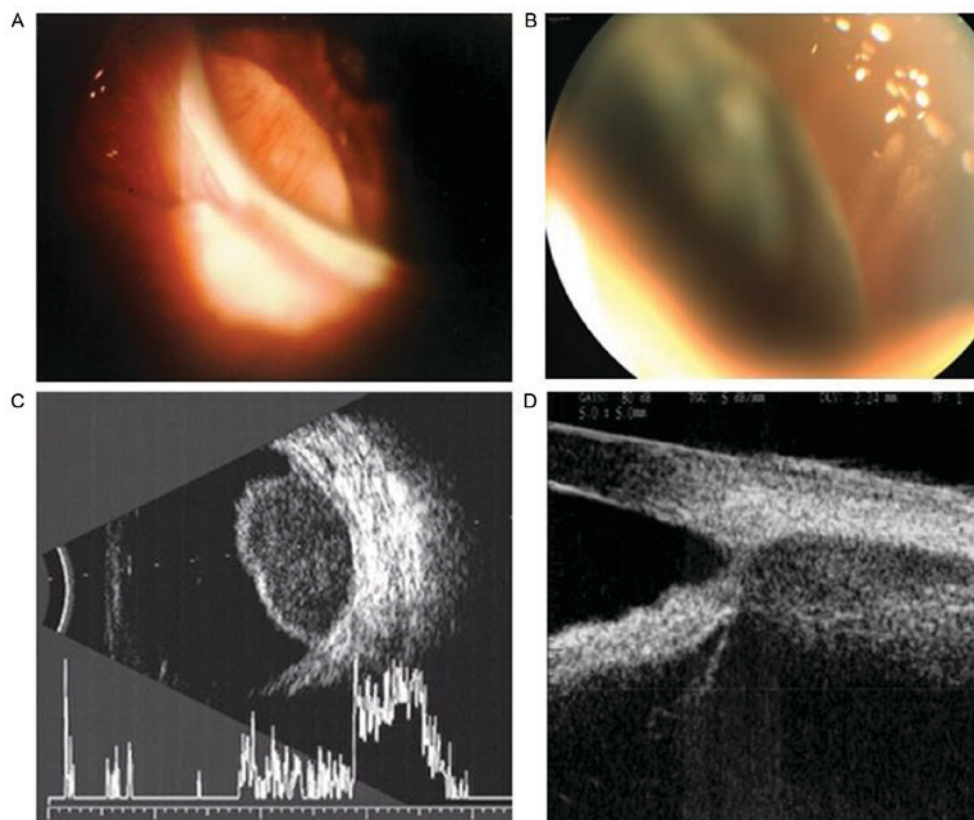


Figure 2. (A) Colored slit-lamp imaging showed a large, prominent, pink, solid lesion that was rich in blood vessels in the anterior chamber prior to the ciliary body from the 6 to 9 o'clock position in the left eye. (B) Fundus imaging revealed a nasal choroidal tumor and asteroid hyalosis. (C) Ultrasonography revealed asteroid hyalosis in the vitreous humor and a 16.7-mm wide and 11.2-mm high hypoechoic mass. (D) Ultrasound biomicroscopy showed a giant mass on the inferior nasal quadrant of the ciliary body, with low-to-middle grade acoustic reflectivity.

postoperative day 5 showed that the giant iridociliary mass had been completely resolved (Fig. 3). The patient's BCVA was 20/40, with an IOP of 10 mmHg. The patient was followed up for 16 months and was disease-free until the last follow-up examination, with a BCVA of 20/20.

Discussion

Intraocular schwannoma is an extremely rare benign neoplasm that arises from Schwann cells. To date, there has been no report of malignant intraocular schwannoma (5,16,18). A confirmed

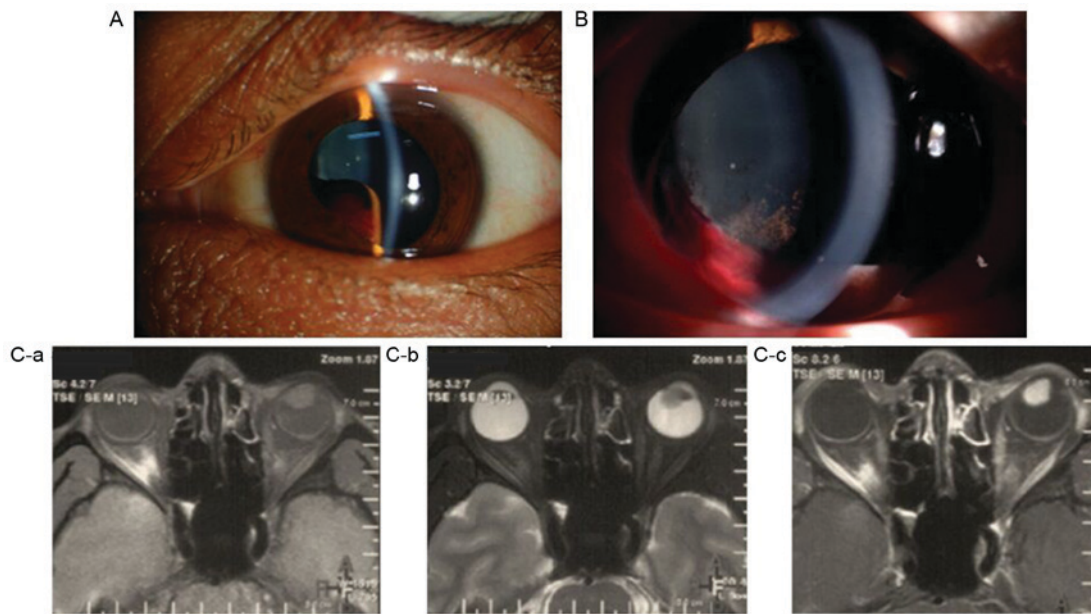


Figure 3. (A) Colored slit-lamp imaging showed a highly prominent brown, avascular, solid homogenous mass in the left eye. (B) Slit-lamp imaging on postoperative day 5 showed no tumor through the dilated pupil following local excision surgery. (C) Magnetic resonance imaging revealed a mass with a clear boundary in the inferior nasal quadrant of the left ciliary body. (C-a) Standard T1WI scans showed an equal signal. (C-b) T2WI scans showed equal or slightly high intensity signal. (C-c) Contrast-enhanced T1WI scans showed homogenous enhancement. WI, -weighted imaging.

diagnosis depends on the immunohistochemical analysis of biopsy results, which can distinguish schwannoma from other spindle-cell tumors. Intraocular schwannoma often disguises itself as an amelanotic choroidal melanoma in the clinic. In a previous report, 44% of eyes with schwannoma were reported to have been enucleated, since the clinical assessment tended to be that of a malignant mass (13). Local lesion resection can successfully preserve a viable globe. Complete lesion resection results in visual acuity being preserved and a normal IOP. In the present case series, the schwannomas were isolated tumors with no association with multisystem disorders, and all the three cases underwent local resection and retained the eyeball.

Case 1 is typical in that the patient was preliminarily diagnosed with choroid and ciliary body melanoma upon medical examination and only confirmed with a cilio-choroidal schwannoma on histopathological examination. Case 2 showed a prominent, pink, solid lesion that was rich in blood vessels, with a pathological diagnosis of schwannoma. The lack of tumor pigmentation is not diagnostic; for example, leiomyoma, melanoma and other tumors can be amelanotic, while schwannoma can be deeply pigmented. Histopathological examination is required for a definitive diagnosis. Case 3 is the only case in which the ciliary body was involved, and following a local excision, the BCVA was significantly improved.

In conclusion, choroidal schwannoma has a variety of clinical manifestations. The most common symptom is decreasing vision without pain, but others include proptosis of the eye, the limitation of ocular movement, leukocoria and occasional pain, as described in previously reported cases (5). However, all the clinical features are attributable to the expansile growth of the tumor and the oppression of the surrounding structures. Although clinical features and findings on ultrasonography,

indocyanine green choroidal angiography, fundus fluorescein angiography, MRI and computed tomography in a schwannoma can provide assistance in differentiating these tumors from others, a definite differentiation is often not possible prior to histopathological examination (19). In certain previous cases, eyeball enucleation has been performed due to a malignant melanoma diagnosis or due to the rapid progression of symptoms, which was considered malignant, and only subsequent histopathological examination of the surgical specimen has revealed a benign tumor. As cytologically benign tumors, intraocular schwannomas only require treatment to prevent the visual loss that results from their enlargement. In cases where the clinical features are not typical of melanoma, such as the presence of cystic components or amelanotic lesions, we recommend performing a surgical excision followed by immunohistological analysis to confirm the features of the neoplasm, whether benign or malignant, prior to considering enucleation. Thus, the present study indicates that pathological biopsy is required for diagnosis and the optimal therapy for intraocular schwannoma is local resection. A reliable non-invasive examination is now required to obtain a diagnosis and guide the subsequent treatment, in order to reduce the final enucleation rate.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

JL contributed to the conception and constructive discussion of the case series. YY, YC and KW contributed to analysis of the data, and the preparation and writing of the manuscript. YY contributed to the search for computerized databases and patient medical records. KS and DS contributed to the pathological diagnosis and description.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from all patients.

Competing interests

The authors declare that they have no competing interests.

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