Short Communication

Eye Tumors Misdiagnosed as Glaucoma

Min Yang[1], Wei Wang[2], Jian-Hua Yan[1], Xing-Yi Li[2], Min-Wen Zhou[2], Wen-Bin Huang[2], Xiu-Lan Zhang[2]

[1]Department of Strabismus and Amblyopia, State Key Laboratory of Ophthalmology, Sun Yat-sen University, Guangzhou, Guangdong 510060, China
[2]Department of Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-sen University, Guangzhou, Guangdong 510060, China

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Introduction

Eye tumors can show diverse clinical signs. They can be misdiagnosed as glaucoma because of red eye, pain, severe headache, elevated intraocular pressure (IOP), even adhesion of the angle of the anterior chamber. In a study by Shields *et al*.,[1] 58 in 144 (40%) of patients with iris melanoma were diagnosed as glaucoma on their initial visit. However, special clinical characteristics, ophthalmic examination, and imaging technology can assist in making the right diagnosis. Ultrasound examinations, high-resolution ultrasound biomicroscopy (UBM), fluorescein angiography, optical coherence tomography, computerized tomography (CT), magnetic resonance imaging (MRI), and fine-needle aspiration biopsy are technologies that may help with early tumor detection. In this study, we highlighted the importance of correctly diagnosing tumor-related glaucoma through the review of nine cases that were initially misdiagnosed as glaucoma.

Methods

The total of 9 patients with eye tumors were misdiagnosed as glaucoma at their first visit. They were all seen at the Eye Hospital, Zhongshan Ophthalmic Center of Sun Yat-sen University, and were retrospectively reviewed from 1997 to 2013. These patients included one case of choroid melanoma, one case of iris and ciliary body melanoma, one case of ciliary body medulloepithelioma, one case of intraocular metastases, one case of optic nerve sheath meningioma, and four cases of retinoblastoma. They underwent forms of imaging technologies such as ultrasound B-mode scan (B-scan), UBM, CT, or MRI. Eye tumors were confirmed by pathological examination, except case 5 who was diagnosed by a history of brain meningioma and the result of a CT, and he was treated by radiotherapy instead of a tumorectomy in another hospital. General information such as medical history, age, sex, and clinical data of the involved eyes from all patient records were available. Information on clinical symptoms, signs, results of imaging technology, drug therapy/surgical management, and pathology was collected as well. Based on the collected data, the reasons for misdiagnosis and the methods for making the right diagnosis of eye tumors were analyzed.

This study was approved by the Ethical Review Committee of Zhongshan Ophthalmic Center of Sun Yat-sen University. All participants in this study received a detailed explanation about the study and signed an informed consent form to agree to the analysis of their information in accordance with the principles embodied in the *Declaration of Helsinki*.

Results

The clinical data of all cases were shown in Table 1. All the patients were unilaterally involved. The most common symptoms were decreased visual acuity, eyelid swelling, red eye, pain or headache, nausea, vomiting, and increased IOP. Conjunctival and ciliary congestion, corneal edema, mydriasis, and iris neovascularity occurred in some cases. Because these symptoms and clinical signs were similar to glaucoma, all these cases were misdiagnosed as primary or secondary glaucoma.

Among them, case 1 was referred to the emergency department due to her symptoms and was diagnosed as primary acute angle-closure glaucoma in the first visit [Figure 1a]. However, on the 2nd and 3rd days, a rapid progression, hyphema, and obvious chemosis appeared [Figure 1b and 1c]. Considering the curious nature of this phenomenon, further examination was undertaken. A large mass was discovered by B-scan ultrasound [Figure 1d] but not with UBM [Figure 1e]. At the same time, MRI prompted the possibility of choroid melanoma [Figure 1f]. The patient underwent enucleation and was diagnosed with choroid melanoma of the right eye after a pathological evaluation. Case 2 was diagnosed with primary chronic angle-closure glaucoma. What was special

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Address for correspondence: Dr. Jian-Hua Yan, Department of Strabismus and Amblyopia, Zhongshan Ophthalmic Center, State Key Laboratory of Ophthalmology, Sun Yat-sen University, Guangzhou, Guangdong 510060, China
E-Mail: yanjh2011@126.com

Table 1: The clinical data of nine cases

Case/age (years)/sex/ side	Clinical signs in initial visit	Symptoms	IOP (mmHg)	Primary diagnosis	Ultrasound biomicroscopy findings	B-scan in the initial visit	CT/MRI	Last diagnosis
1/60/ female/right	Hydropic cornea, mixed congestion, mydriasis	Swelling, pain, headache, vomiting	61	Primary acute angle-closure glaucoma	Anterior chamber angle closed	Moderate low echogenic mass	An intraocular mass	Choroid melanoma
2/37/ female/left	Adhesion of anterior chamber angle from 10’ to 1’clock, anterior synechia and brown nodules from 10’ to 1’clock of iris	Decreased visual acuity	13†	Primary chronic angle-closure glaucoma	An iris-ciliary body mass from 10' to 1' clock	Vitreous opacities	Incrassation of iris and ciliary body	Iris-ciliary body melanoma
3/6/ male/left	Corneal edema, pigment KP (++), anterior synechia from 3’ clock to 6’ clock, mydriasis	Swelling and pain	59	Secondary glaucoma	N/A	Vitreous opacities	N/A	Ciliary body medullaepit-helioma
4/66/ male/right	Corneal edema, nodes and neovascularization on the surface of the iris, irregular pupil	Decreased visual acuity and pain	39.5	Secondary glaucoma	Ciliary body edema, one mass echo in irisciliary body	N/A	N/A	Intraocular metastase microgliaoma
5/30/ male/right	Hydropic cornea, neovascular on the surface of iris, mydriasis, cataract	Invisibility, red-eye	48	Secondary glaucoma	Anterior chamber shallow and closed	Lung membrane, tractional retinal detachment	Thickening of the optical nerve, sella turcica was involved	Optic nerve sheath meningioma
6/7/ male/left	Hydropic cornea, neovascularity in the surface of iris, mydriasis, cataract	Pain, red eye, decreased vision	59	Primary glaucoma	N/A	Irregular echogenic mass Intraocular	Thickening of the orbit and calcification	Retinoblastoma
7/5/ female/left	Conjunctival congestion, hydropic cornea, neovascularity in the surface of the iris	Pain, red eye, headache, nausea, vomiting	–*	Secondary glaucoma	N/A	Irregular echogenic mass, a strong echo in the mass	N/A	Retinoblastoma
8/9/ female/left	Conjunctival congestion, suet shape KP (++), hypopyon	Pain, red eye, decreased vision	25.3	Secondary glaucoma	A large amount of attachments on the surface of the iris	Vitreous opacity and a moderate echogenic mass	No obvious intraocular mass	Retinoblastoma
9/4/ female/left	Corneal opacity, iris neovascular, shallow anterior chamber and cataract	Strabismus, leukocoria	42	Secondary glaucoma	N/A	A solid light echo mass	A mass and calcium in the orbit	Retinoblastoma

*IOP cannot be measured by NCT because of imparity, but finger measurement was T+2. †IOP was controlled after using three kinds of anti-glaucoma medicines. N/A: The technology not performed; CT: Computerized tomography; MRI: Magnetic resonance imaging; IOP: Intraocular pressure, which was measured by NCT; KP: Keratic precipitate.

about case 2 was that brown nodules in the iris and many pigment depositions were found in the trabecular meshwork in the corresponding place of the anterior synechia under a slit-lamp [Figure 1g] and gonioscope [Figure 1h]. Then, a UBM [Figure 1i] was immediately conducted and found a 4.5 mm × 3.5 mm iris-ciliary body mass. On the other hand, a B-scan [Figure 1j] did not find an obvious mass. The patient received local tumor removal, and the diagnosis of iris-ciliary melanoma was confirmed by pathological examination. After the surgery, the patient obtained a good result [Figure 1k].

Unlike case 1 and case 2, antiglaucoma surgery in case 3 and case 4 was performed before the tumors were noted. The IOP of case 3 was raised after a trauma, and the IOP continued to increase even after six antiglaucoma surgeries were performed. When he came to us, the diagnosis of secondary glaucoma was made. The B-scan found only vitreous opacities. A staging surgery of a glaucoma valve implantation combined with trabeculectomy surgery was performed on the patient because of the uncontrolled IOP. When he visited us again after a long hiatus, an intraocular mass had been found in another hospital. Off white opacities in the anterior chamber and yellow-gray apophysis in the fundus of the left eye were found by slit-lamp and direct ophthalmoscope. At this time, a B-scan showed a moderate to low echogenic intraocular mass and a UBM also confirmed a mass both in the anterior chamber and behind the iris. An intraocular mass excision biopsy was performed, and the pathology demonstrated it was a ciliary body medulloepithelioma of the left eye. This patient finally underwent enucleation.

In case 4, symptoms and clinical signs caused the diagnosis of secondary glaucoma, and a glaucoma valve implantation surgery was performed. The IOP of this patient was controlled

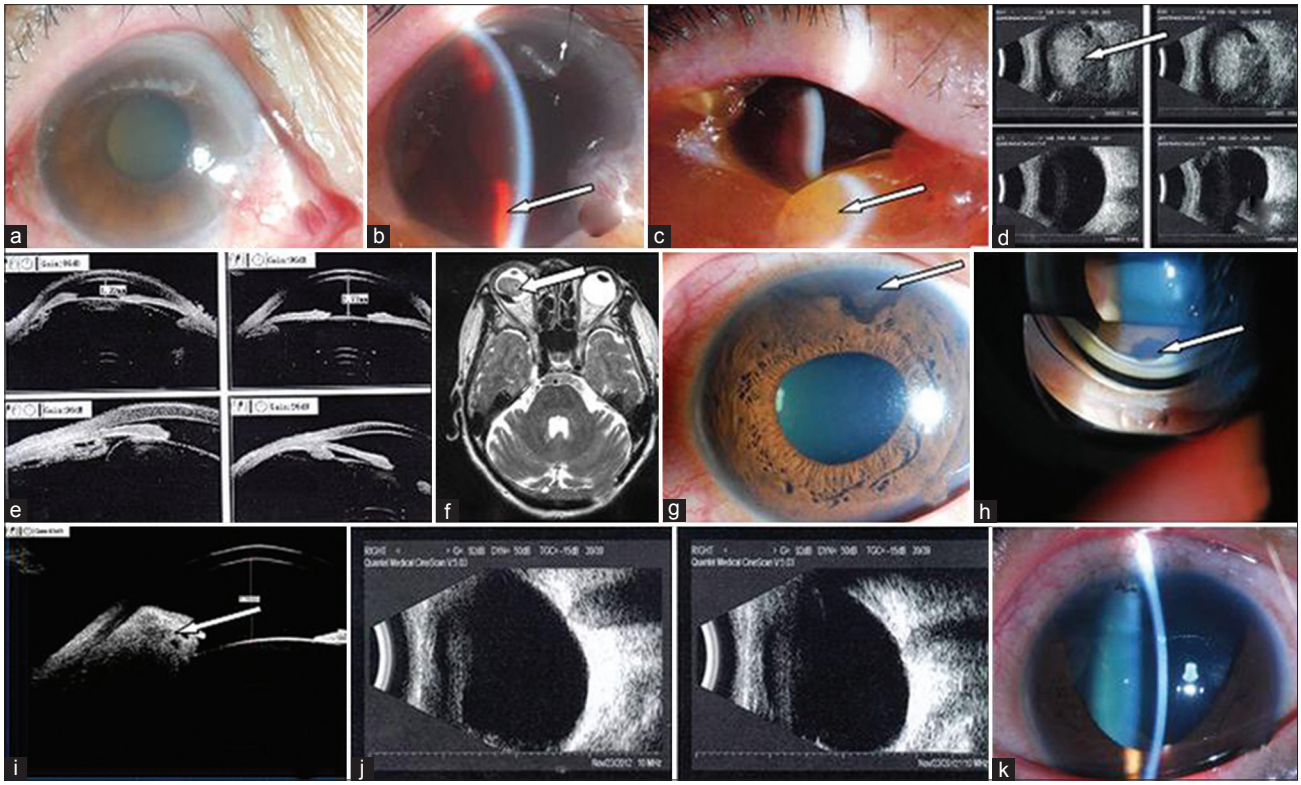

Figure 1: A patient with choroid melanoma appeared as primary acute angle-glaucoma in the first visit. The initial signs of the patient were red eye, hydropic cornea, mixed congestion and mydriasis (a); hyphema appeared on the 2nd day (b, arrow). Obvious chemosis on the 3rd day after initial symptoms appeared (c, arrow), and at the same time, a moderate-low echogenic mass found by B-scan (d, arrow), while the ultrasound biomicroscopy (UBM) did not find a mass (e). An intraocular mass was detected by magnetic resonance imaging (f). Another patient with iris-ciliary body melanoma misdiagnosed as primary chronic angle-closure glaucoma. A neoplasm could be seen at about from 10' clock to 1'clock through slit-lamp (g). In the corresponding place, a nodule was detected by gonioscope (h). A mass in the iris and ciliary-body was found via UBM (i). Meantime, UBM found the adhesion of the anterior Chamber angle from 10' clock to 1'clock; on the other hand, the mass was not found by B-scan (j). The patient had a good result after an iris-ciliary body tumor reduction surgery (k).

temporarily after the surgery. However, the patient came to us again after 2 months because of the mass in the iris found by another hospital. A slit-lamp showed exudation in the anterior chamber, nodules, and neovascularization in the surface of the iris and a wide range of the synechia. A suspect diagnosis of metastatic cancer was considered after an iris tumorectomy. As expected, the patient was diagnosed with cerebral gliomas and underwent a tumorectomy in another hospital. What surprised us most was that a new tumor appeared a week later at the temporal conjunctiva of the right eye. To resolve the severe pain of the eye, enucleation was performed on the patient.

The diagnosis of case 5 was neovascular glaucoma when he came to us. However, the patient had a history of cerebral meningioma, which was confirmed by pathology, and had a previous tumor surgically removed. In addition, a mild protopsis of the eye was showing. Based on this, a follow-up CT examination found a tumor in the brain and orbit. The CT scan showed a thickening of the optical nerve and sella turcica was involved, but a clear diagnosis between schwannoma and meningioma was not made. Considering the history of meningioma, a diagnosis of optic nerve sheath meningioma was made with a high level of certainty. In the end, this patient was treated by radiation instead of a tumorectomy in another hospital.

All the patients with retinoblastoma (cases 6–9), who were diagnosed with secondary glaucoma or primary glaucoma at the first visit, a correct diagnosis was made before surgery using B-scans and CTs. In all of the patients, an irregular moderate echogenic mass was revealed by B-scan and calcification appeared in 1 of 4 cases. The pathological result after an enucleation surgery proved the diagnosis of retinoblastoma in this case.

Discussion

Intraocular tumors, whether primary or metastatic, can masquerade as secondary or primary glaucoma. Many factors lead to the diagnosis of glaucoma in patients with intraocular tumors, including solid tumor invasion-related outflow obstruction, infiltrative tumor-related outflow, trabecular meshwork seeding, neovascularization, and angle closure due to compressive and rotational inflammation and pseudo-inflammation.[2]

Clinical symptoms and signs of tumor-related glaucoma are red eye, eye pain, severe headache, elevated IOP, even adhesion of the angle of anterior chamber, and a shallow anterior chamber, which lead to the diagnose of primary glaucoma or secondary glaucoma. On this occasion, if

there was no alert for further examination, anti-glaucoma surgery may have been performed to reduce the IOP. Barsky *et al*.[3] considered distinctive ocular symptoms, markedly elevated IOP, acquired iris heterochromia, and the failure of appropriate treatment as indicating an underlying malignancy to secondary glaucoma. In our study, all cases were monocular, and only one case had a controlled IOP after anti-glaucoma treatment. Hyphema and hypopyon are rare in primary glaucoma, but can appear in secondary glaucoma due to various diseases. Glaucoma, even acute primary angle-closure glaucoma, rarely appears to have acute progress like case 1. The condition of this case-affected eye deteriorated quickly while the other eye remained normal. In case 2, the brown nodules on the surface of the iris and the anterior synechia appearing in the same place as the nodules found by slit-lamp and gonioscope was unique to glaucoma. As to case 3, it was odd that this case presented uncontrolled IOP, even after numerous anti-glaucoma surgeries. These were the clinical clues of suspected eye tumor-related glaucoma. A history of primary cancer and the mass appearing on the surface of the iris 2 months after diagnoses were unique to case 4. Similar to case 4, case 5 also had a history of the brain meningioma; moreover, the symptom of protopsis was rare in glaucoma. Based on these unusual clinical signs accompanying glaucoma, ophthalmologists should be vigilant to cases such as those described above, and further examinations should be undertaken.

However, it is still difficult to find the tumor due to its dormant development in some cases, and this is especially true for tumors behind the iris and those in the ciliary body. In this respect, imaging technology, such as B-scan ultrasonography, UBM, CT, or MRI can discover eye tumors and avoid misdiagnosis. UBM has an advantage of precisely representing the anterior segment structure and is, therefore, useful for analyzing the anterior segment mass.[4] Therefore, UBM could be the best choice for detecting an iris and ciliary body mass. Since the UBM has limited-distance detection with regard to a tumor in the posterior segment and in an orbit, B-scan, CT, MRI, or fluorescein angiography can be the preferred choice. These imaging technologies are often necessary for the right diagnosis. However, in some cases with tumor-related glaucoma, you do not find the tumor by examinations mentioned above, especially in the initial stage of tumor growth; like case 3 and case 4 in our study. Rigorous follow-up and repeated imaging examination can lead to a relatively early diagnosis.

Anti-glaucoma surgery may be undertaken for tumor-related glaucoma before discovery of the tumor. This type of action is dangerous, especially for a filtering surgery, as tumor cells may transfer to outside the eyeball through the filtering route. Pasternak *et al*.[5] reported a patient with tumor-related glaucoma, where subconjunctival tumor spread occurred after glaucoma filtering surgery. In our study, a metastatic cancer was found in the conjunctiva in one case. It was considered to be due to the spread of tumor cells through the glaucoma valve. Hence, it is very important not to delay the diagnosis and therapy of primary tumors.

In conclusion, many tumors, regardless if they are primary or metastatic, can appear as secondary or primary glaucoma and be misdiagnosed due to the many reasons described in this study. However, misdiagnosis can be avoided by some clues and evidence, such as a history of systemic tumor, unexpected fast progress, pseudo-hypopyon, mild protopsis, small iris nodules, and ambiguous iris neovascularization. Careful ophthalmic examination and the use of imaging technology may assist finding the correct diagnosis. Rigorous follow-up and repeated imaging examination can lead to an earlier diagnosis.

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