Resection of uveal melanocytoma: clinicopathological correlation

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SUMMARY Four patients had pigmented lesions in the anterior uveal tract and choroid which presented clinically as malignant melanomas. All the lesions were successfully removed by local excision. Histopathological studies showed the tumours to be melanocytomas, indicating that enucleation or irradiation would have been contraindicated. The 3 patients with iris and ciliary body melanocytomas continue to maintain corrected visual acuities of 20/30 or better. In the patient with choroidal melanocytoma central visual acuity was compromised owing to cystoid macular oedema. All 3 melanocytomas involving the anterior segment were located inferiorly. Biomicroscopically, they were chocolate coloured (not black) and resembled malignant melanomas of the same location. The choroidal melanocytoma also resembled a malignant melanoma by ophthalmoscopic and angiographic criteria, and did not have the jet black or homogeneous pigmentation that characterises most melanocytomas of the disc.

Melanocytoma was first described as a distinct clinicopathological entity by Zimmerman and Garron¹ in 1962. They identified it as a type of benign naevus involving the optic nerve head. Characteristically it is a slow-growing maximally pigmented tumour that occurs preponderantly in noncaucasians or deeply pigmented individuals. Although the tumour may give the clinical and histopathological impression of infiltrating the ocular structures,²⁻⁴ no evidence of metastasis has ever been reported. Melanocytoma is classically located at the optic disc,² although rarely it has been described in the choroid,⁵ ciliary body,⁶ and iris.⁷

Differentiation from other pigmented tumours is often possible at the optic disc because of the rarity of other pigmented lesions in this location.² However, differentiation from malignant melanomas occupying the choroid, ciliary body, or iris is extremely difficult on clinical grounds alone. Unfortunately the final diagnosis is usually made on histopathological examination. Any clinical observation that distinguishes these tumours is of obvious importance and could prevent unnecessary enucleation or irradiation.

We here report 4 cases of histologically confirmed

melanocytoma of the iris, ciliary body, and choroid which clinically appeared to be malignant melanomas. These tumours were successfully resected with maintenance of good visual acuity in the operated eyes. Most of the operations were performed by one of us (G.A.P.).

Fig. 1 Case 1. Goniophotograph of inferior aspect of left eye. Pigmented lesion extends between 6 and 8 o'clock (arrows).

Case reports

CASE 1

A 35-year-old white woman was seen in May 1975 with a red, irritated left eye of 2 days' duration. At the time of the initial examination her vision was 20/30 in each eye. The right eye was entirely normal. The left conjunctiva showed 2+ injection. The cornea was clear except for a small old scar at the 8 o'clock position.

The anterior chamber was clear, and the pupil was round and reactive. There was a 3×1 mm pigmented tumour in the anterior chamber angle from 6 to 8 o'clock (Fig. 1). On either side of the lesion were freckles on the iris. Gonioscopy revealed heavy pigmentation of the inferior angle. The tumour itself was touching the back of the cornea in the angle. The lens and ocular media were clear. The retina was normal. The intraocular pressure in each eye was 16 mmHg.

Transillumination showed an opaque dark brown lesion in the angle which extended into the ciliary body for about 3 mm. The possibility of malignancy was discussed with the patient, and on 30 June 1975 preparatory cryotherapy was performed on the sclera around the tumour. Two rows of cryocoagulation were applied from the 5.30 to 9 o'clock positions in a semicircular fashion. Then on 26 August 1975 an iridocyclectomy was performed according to the technique described below. The lens was left in situ. The postoperative course was uneventful, and on 27 October 1975 visual acuity was 20/40 with a pinhole. The patient has maintained good visual acuity, and the lens has remained clear. Six years later the visual acuity was 20/30 with correction, and the eye was uninfamed.

Histopathological examination. The gross specimen consisted of an eye-wall fragment containing corneo-scleral tissue, iris, and ciliary body. A heavily pigmented tumour mass was noted in the ciliary body and grossly infiltrating the root of the iris.

By light microscopy the tumour was composed of tightly packed, maximally pigmented round cells. On bleached preparations the cells were large and round

Fig. 2 A. Uniformly, densely pigmented melanocytoma of ciliary body and iris root. CB, ciliary body. Asterisk, lamellar corneal resection. TM, trabecular meshwork (haematoxylin and eosin, ×12). B. Densely pigmented tumour cells without identifiable cellular details, infiltrating angle structures. TM, trabecular meshwork. C, cornea (haematoxylin and eosin, ×97). C. High-power view of cells infiltrating iris root (haematoxylin and eosin, ×97). D. On bleached preparation the tumour is composed of packed cells with abundant cytoplasm and centrally placed benign-appearing nuclei (haematoxylin and eosin, bleached with potassium permanganate, ×227).

with abundant eosinophilic cytoplasm and uniformly ovoid, benign appearing nuclei (Fig. 2). In the more peripheral areas of the tumour some of the cells became more spindle shaped; a few cells contained prominent nucleoli. Mitotic figures or other evidence of anaplasia were not observed. Newly formed blood vessels within the tumour were not identified. The final diagnosis was ciliary body melanocytoma infiltrating the root of the iris.

CASE 2

In September 1978 a 60-year-old white man was referred to us after his local ophthalmologist noticed a gradually enlarging pigmented lesion of the left iris. At the time of the initial examination his visual acuity was 20/30 bilaterally. The right eye was within normal limits. The left eye showed a dark brown raised lesion in the angle between the 6 and 8 o'clock positions (Fig. 3). The lesion was composed of two elevations connected by a bridge. Slit-lamp examination showed that the lesion was touching the back of the cornea. Gonioscopy showed closure of the angle at the site of the lesion with heavy pigment dusting of the inferior angle. The pupil was round and reactive. The lens showed nuclear and cortical opacities. The media were otherwise clear, and the retina was normal. The intraocular pressure was 16 mmHg in the right eye and 12 mmHg in the left eye. The results of a systemic evaluation were normal. Fluorescein angiography of the pigmented lesion showed no fluorescein leakage from the tumour mass. Transillumination of the lesion, which was opaque, disclosed a 2 mm extension of the tumour into the ciliary body.

Because the tumour increased in size, and iridocyclectomy with lensectomy was performed on 12 November 1978.

The histopathological diagnosis was melanocytoma. The postoperative period was uneventful.

Fig. 3 Case 2. Goniophotograph of inferior angle, left eye. Pigmented lesion extended between the 6 and 8 o'clock positions (arrows).

With the use of a contact lens the patient had a visual acuity of 20/30 when last examined on 14 September 1981, 3 years postoperatively.

Histopathological examination. The gross specimen consisted of a fragment of eye-wall containing

Fig. 4 Top: Melanocytoma of iris. Note darkly pigmented cells infiltrating angle structures and anterior aspect of ciliary body (haematoxylin and eosin, $\times 37$). Bottom: Bleached preparation of tumour described above shows plump cells with abundant cytoplasm and centrally placed benign-appearing nuclei (haematoxylin and eosin bleached with potassium permanganate, $\times 498$).

corneoscleral flap, iris, and ciliary body. A small darkly pigmented tumour measuring 3×2 mm in its largest diameter obscured the angle structures and limbal corneal tissue.

On light microscopy the tumour was composed of tightly packed avascular clusters of round, uniformly, and heavily pigmented cells. A bleached preparation showed that the cells were plump and polyhedral, with abundant cytoplasm and ovoid to round nuclei with open, uniformly clumped chromatin (Fig. 4).

Single tumour cells were irregularly shaped, and some contained conspicuous nucleoli. The surgically resected margins were free of tumour cells. The diagnosis was iris melanocytoma infiltrating angle structures and ciliary body.

CASE 3

A 58-year-old white woman was referred to us in July 1978 for examination of a pigmented anterior chamber mass in the left eye. This lesion was noticed

Fig. 5 A. Heavily pigmented melanocytoma on anterior-most aspect of ciliary body. Note tumour infiltrating ciliary processes (arrows). CB, ciliary body (haematoxylin and eosin, ×30). B. Same tumour infiltrating iris stroma. IPE, iris pigment epithelium. DM, dilator muscle (haematoxylin and eosin bleached with potassium permanganate, ×100). C. High-power view of ciliary body melanocytoma showing cells with abundant cytoplasm and round centrally placed nuclei (haematoxylin and eosin bleached with potassium permanganate, ×507). D. Tumour cells in angle structures appear to be restrained from growth into cornea by Descemet's membrane. TM, trabecular meshwork (haematoxylin and eosin bleached with potassium permanganate, ×85).

Fig. 6 Wide-angle photograph of choroidal lesion surrounded by xenon photocoagulation marks. Arrow corresponds to resected margins in Fig. 9.

Fig. 7 Enlarged view of tumour mass. Arrows correspond to tumour margins.

by an optometrist to whom she had gone for contact lenses. She denied previous ocular symptoms. Her past history included excision of a naevus from her groin 15 years earlier.

Ocular examination showed a visual acuity of 20/20 with correction in the right eye and 20/40 in the left eye. The right eye was entirely normal. The left eye showed an obvious chocolate brown lesion on the iris that extended into the anterior chamber between the 5 and 6.30 positions. The pupil was slightly eccentric, round, and reactive. The iris lesion did not transilluminate and showed a 2 mm extension into the ciliary body. Slit-lamp examination showed the mass to be composed of two touching mounds that were in contact with the corneal endothelium in the far periphery. There was a dense posterior subcapsular and cortical cataract inferiorly in the left eye. On gonioscopy the mass touched the cornea inferiorly and obscured the entire trabecular meshwork between the 5 and 6.30 positions. The mass extended behind the iris and indented the equator of the lens inferiorly, which produced cataractous changes in the subcapsular region.

The remainder of the examination gave results within normal limits. The intraocular pressure was 17 mmHg in the right eye and 19 mmHg in the left. Iris fluorescein angiography revealed no dye leakage from the mass. A diagnosis of malignant melanoma was made. An extensive search for metastases was negative.

On 21 July 1978 the iris and ciliary body tumour was

removed by iridocyclectomy with deep lamellar resection of sclera and cornea, as described below. The lens was left in position and the vitreophage was used to clear vitreous from the wound margins. The postoperative period was uneventful, but the visual acuity was gradually compromised by progressive development of cataract. On 17 April 1979 an extracapsular extraction of the cataract was performed through a superior limbal incision. When she was last seen in May 1981, her visual acuity in this eye was 20/30 with correction.

Histopathological examination. The gross specimen consisted of a 7.5×6×5 mm triangular shaped fragment of eye-wall, containing corneal tissue, sclera, ciliary body, and iris root. The anterior-most aspect of the ciliary body was occupied by a dark and heavily pigmented tumour mass that appeared to extend to the lateral margins of resection.

Histologically the tumour was composed of uniformly pigmented clusters of large, polyhedral, maximally pigmented cells, which in a bleached preparation showed abundant eosinophilic cytoplasm with centrally placed, benign-appearing, round nuclei (Fig. 5). Anteriorly the tumour cells had obliterated the angle structures and infiltrated the iris stroma. Some clusters of tumour cells appeared to be restrained from growth into the corneal stroma by Descemet's membrane (Fig. 5D). Newly formed blood vessels within the tumour mass were not observed. As noted in the gross specimen, some of the tumour cells were present on both lateral resected

Fig. 8 Diffuse leakage of fluorescein is seen in the tumour mass.

Fig. 9 Postoperative view of resected area (totally avascular and black). Arrow corresponds to the superotemporal arcade.

surgical margins. The final diagnosis was ciliary body melanocytoma that infiltrated angle structures and extended to the lateral margins of surgical resection.

CASE 4

A 64-year-old man was seen in February 1981 after referral by his ophthalmologist for examination of a tumour in his left eye. The ophthalmologist had originally noted the tumour in December 1980, and the patient was referred to us because of growth in its size.

At the time of our examination the vision was 20/30 in both eyes. The patient had no visual symptoms. The anterior segments were normal. The fundus had a round, dark grey, uniformly pigmented lesion approximately 10 mm in diameter and 3 mm in thickness in the superior choroid (Figs. 6 and 7). The tumour extended in the 12 o'clock meridian from a point 4 disc diameters superior to the disc, totally posterior to the equator. Results from the rest of the examination were unremarkable. Fluorescein angiography showed double circulation with diffuse leakage of the dye in the tumour mass (Fig. 8), consistent with malignant melanoma. Ultrasonography with both a- and b-scan modes showed the tumour to be a solid mass. The findings of low internal reflectivity were consistent with a malignant melanoma. Transillumination of the tumour disclosed blockage in the transmission of light.

The patient was advised of the possibility of the lesion being malignant and of the various types of treatment. She elected to undergo eye-wall resection.

In March 1981 preparatory xenon arc photocoagulation was applied to the attached retina surrounding the tumour. This was repeated on 13 March 1981.

On 13 April the patient was admitted for a resection of the tumour. The visual acuity at admission was 10/70 in the left eye. There were wrinkling of the internal limiting membrane and oedema of the optic nerve head and macula.

On 15 April 1981 an eye-wall resection was performed without any complications (Fig. 9). The postoperative period was uneventful. Follow-up 8 months after surgery revealed a quiet eye with a visual acuity of 4/200. The anterior segment was clear, the lens was clear, and the retina was attached. There was oedema at the optic nerve head and the macula, which accounted for the reduced visual acuity.

Histopathological examination. The gross specimen was of an eye-wall fragment consisting of sclera, choroid, and retina. A heavily pigmented tumour mass was located in the choroid. There was no obvious infiltration of the sclera.

By light microscopy the tumour was seen to be composed of a uniformly pigmented naevoid mass. In a bleached preparation the cells were plump and polyhedral, with abundant cytoplasm, round nuclei, and uniformly clumped chromatin. There was no microscopic infiltration of the sclera. The histopathological diagnosis was melanocytoma.

The following is a description of surgical techniques developed by one of us (G.A.P.) for the treatment of uveal tumours.

SURGICAL TECHNIQUES

Iris and ciliary body tumours

All the operations were performed with the patient under retrobulbar anaesthesia. Good exposure of the globe was obtained with interrupted 4-0 black silk sutures, which were passed through the lid margins and tied to the surrounding drapes. A 360° limbal peritomy was then made with relaxing incisions at 3 and 9 o'clock. At each corner of the conjunctiva 4-0 silk marking sutures were placed. After cleaning any episcleral adhesions, bridle sutures were passed under the 4 rectus muscles. A Peyman cyclectomy basket was selected that conformed to the curvature of the globe. The basket was secured in position surrounding the tumour by means of running 5-0 Dacron sutures.

Transillumination was then performed, and the extent of the tumour on to the ciliary body marked on the sclera with a marker. With a no. 64 Beaver blade a partial-thickness scleral groove was made 3 mm from the scleral margins of the tumour. A semicircular flap of partial-thickness sclera was dissected from the limbus. With the blunt tip of the diathermy a semicircular arc of diathermy was placed over the partial-thickness sclera to surround the mass of the tumour over the ciliary body, leaving margins of at least 2 mm. This plane of the diathermised groove was then deepened with penetrating diathermy. This procedure was repeated until the uvea became visible.

The partial-thickness sclera was lifted backwards, and a corneoscleral groove was made at the limbus and deepened gradually until the anterior chamber was entered. Sector iridectomy was then performed. The uveal incisions were carried back to the posterior border of the tumour. The specimen was removed, and its borders were examined grossly for the distance between the tumour mass and the resected margins. The specimen was then fixed in buffered 4% formaldehyde and sent for histological examination.

If the vitreous prolapsed or the lens was damaged or subluxated, vitrectomy and lensectomy were performed through the opening left by the removal of the tumour. If the lens was hard, it was best removed with a lens forceps or a lens loupe. Vitrectomy was best performed by tightening the preplaced scleral sutures and then by introducing the vitreophage tip through a small gap under the scleral flap.

The rest of the partial-thickness sclera was sutured to the remainder of the sclera with running 9-0 nylon sutures. Air was injected into the vitreous to re-form the globe. The conjunctiva was sutured with 5-0 plain catgut, and atropine and Maxitrol drops (neomycin, polymyxin B, dexamethasone) were instilled.

Choroidal tumours

Surgery was performed with the patient under

general anaesthesia. The eyelids were retracted with 4-0 black silk sutures passed through the lid margins and anchored to the drapes. The rectus muscles were isolated, and 4-0 black silk sutures were passed beneath them. To gain better access to the tumour the superior rectus muscle was detached. Margins of the tumour were delineated by transillumination, and localised cautery marks were applied to the sclera. A half-thickness scleral flap was dissected 1 mm larger than the tumour margins. The partial-thickness flap was dissected with a posterior hinge.

Nonpenetrating and penetrating diathermy was applied round the tumour margin through the scleral bed. The tumour margin was then cut with a pair of scissors along the tract of diathermised tissue, and the tumour was removed. The scleral flap was sutured back into place with 9-0 nylon sutures. A pars plana vitrectomy was performed with the vitreophage in an attempt to clear blood and vitreous near the site of resection. The conjunctiva was sutured back after the superior rectus muscle had been reattached. Subconjunctival injections of 20 mg gentamicin and 20 mg Depo-Medrol (methyl prednisolone) were given, and a patch and shield were applied.

Discussion

Histopathologically the melanocytoma has been clearly defined as a uniformly, maximally pigmented tumour that shows benign cytological features on bleached preparation. They are composed of plump polyhedral naevus cells, with centrally located round nuclei, without mitotic figures. This is in sharp contrast with uveal malignant melanomas, which show irregular pigmentation and variable cellularity. Table 1 delineates some of the histopathological differences between these tumours. In spite of these histological differences the present study of 4 melanocytomas failed to show any clinical information necessary to help differentiate the tumours from uveal

Table 1 *Histological differences between melanocytomas and uveal malignant melanomas*

	<i>Melanocytoma</i>	<i>Malignant melanoma</i>
Cellularity	Plump polyhedral uniform cells	Variable cell types
Pigmentation	Uniformly heavily pigmented	Variable pigmentation
Atypia	None	Present
Nuclear cytoplasmic ratio	Low ratio	High ratio
Blood vessels within tumour mass	None or rare	Common
Ultrastructural presence of giant melanosomes ¹⁴	Yes	No

malignant melanoma preoperatively. Documented growth occurred in all our cases, and was thus not a useful criterion for distinguishing benign melanocytomas from malignant melanomas.

In 2 of the cases with anterior segment lesions fluorescein angiography showed blockage of fluorescein by the pigment in the tumours; there was no visible circulation or pooling of dye, which favours a benign process. Our case of melanocytoma of the choroid (case 4) mimicked the appearance of choroidal malignant melanoma clinically, angiographically, and ultrasonically. Similar cases have been reported by Shields and Font.⁸ Takahashi⁹ reported a case of optic nerve melanocytoma in which a large area of progressive dye pooling was observed.

Since Zimmerman's original descriptions^{1,2} many reports of melanocytoma of the eye have appeared.³⁻⁷ In a review of 907 pigmented ocular tumours Howard and Forrest⁶ could identify 5 cases of melanocytoma. Initially these tumours were thought to be confined to the optic nerve head only. Recently Jakobiec and Silbert¹⁰ in a retrospective study of 189 cases of iris and iris and ciliary body lesions identified 5% of the specimens as melanocytoma. In this series there was no clear-cut correlation between the type of lesion and clinical presentation. Although the reports indicate a preponderance of melanocytoma at the optic nerve head, in 3 of our 4 cases they were located in the anterior uvea.

Previously diagnosis of melanocytomas has been made after enucleation.¹¹ By locally resecting these tumours, however, it is possible to save the eyes. Thus surgical resection is an ideal method of managing such lesions when the correct diagnosis is in doubt preoperatively. When less than 3 clock hours of the iris or ciliary body are involved, local resection of the tumour is technically possible. We believe that excision of the tumour beneath a lamellar flap of sclera is the method of choice. If vitreous loss occurs during surgery, vitrectomy should be performed at the same time with an automated vitrectomy instrument. Vitrectomy can prevent future complications, such as retinal detachment. During the resection of larger iris-ciliary body tumours the lens can be subluxated. It is usually best to remove the lens during the same procedure.

Although melanocytomas are comparatively rare, their occurrence in the eye at locations other than the optic nerve can present a diagnostic problem. In such instances it may be difficult to differentiate clinically a melanocytoma from a malignant melanoma.

Ophthalmoscopic appearance, visual fields, ³²P uptake, ultrasonography, and fluorescein angiography may not be helpful in differentiating melanocytoma of the choroid from malignant melanoma.

Fluorescein angiography of the anterior segment may help in making a diagnosis. In 2 of our cases iris fluorescein angiography showed no circulation in the tumour mass. Blockage of fluorescein by a melanocytoma has also been observed by other investigators.¹² However, Kottow¹³ has pointed out that histologically proved malignant melanomas of the iris have presented absolutely normal angiograms. The biomicroscopic and gonioscopic appearance of the anterior segment tumours was otherwise identical to that of typical malignant melanomas.

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