Metastatic tapioca iris melanoma

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SUMMARY A case of metastatic tapioca melanoma of the iris in a 12-year-old girl is reported. The patient had heterochromia, a red painful eye, and was treated for iritis with secondary glaucoma. In the course of 5 months iris lesions with the clinical appearance of tapioca pudding developed, and biopsy disclosed a melanoma. The eye was immediately enucleated, and pathological examination showed a melanoma with predominantly epithelioid-type cells which had infiltrated the angle, the posterior chamber, and the surgical wounds. Conjunctival extension was noted 10 months after enucleation, and regional lymph node metastases were found 4 months later. Previously reported cases are reviewed and compared with the present case.

Although melanomas are the commonest primary iris tumour (Ashton, 1964), they constitute only a small percentage of uveal neoplasms (Hogan and Zimmerman, 1962; Yanoff and Fine, 1975). Tapioca melanomas of the iris are rarer still, and there is no report of such tumours with epithelioid-type cells. Tapioca melanomas have a distinct clinical presentation and should be considered in the differential diagnosis of iris nodules (Shields *et al.*, 1976). In the past such tumours have been detected mainly between the second and third decades, with an average age of 29 years. All patients were Caucasians, and there was no sex predilection.

This paper reports an iris melanoma in a 12-year-old girl with the following interesting clinicopathologic features: an appearance like tapioca pudding on clinical examination, epithelioid-type melanoma cells on histopathological examination, and extension of tumour to conjunctiva and regional lymph nodes.

Case report

A 12-year-old white girl was first seen by an ophthalmologist in December 1975 for a red and painful condition of the left eye of 2 weeks' duration. Findings included 'severe iritis' and raised intraocular pressure (40 to 50 mmHg by applanation tonometry). The right eye was normal and remained so throughout the course of the disease. A diagnosis of iritis with secondary glaucoma was made, and

the patient was given mydriatics, topical and systemic steroids, and acetazolamide. Despite treatment, the eye remained inflamed, and the intraocular pressure fluctuated at 30 to 40 mmHg.

In February 1976 the patient was seen in consultation and findings in the left eye included: decreased vision (6/9); raised intraocular pressure (34 mmHg by applanation tonometry); small keratic precipitates, flare, and cell reaction (2 to 3+) in the anterior chamber; increased iris pigmentation; pigment on the lens capsule; and extensive pigmentation in the trabecular meshwork. The optic disc was normal (cup/disc ratio 0.4). Skin tests for toxoplasmosis and histoplasmosis, purified protein derivative, streptokinase-streptodornase, and candida gave normal results. The patient was diagnosed as having an idiopathic recalcitrant iritis. Over the next 3 months her left eye remained inflamed with intraocular pressures at 30 to 40 mmHg.

On 3 May 1976 (5 months after onset) visual acuity in the left eye was 6/24, and she had a 1 to 2+ flare and cell reaction in the anterior chamber. The pupil was dilated and nonreactive; the iris showed marked stromal atrophy with nodular elevations, which were particularly notable at 6 o'clock. The lens was covered anteriorly with deposits of pigment and 'inflammatory' cells. The anterior vitreous was free of cellular reaction. A glaucomatous cup was noted (cup/disc ratio 0.8), and the intraocular pressure was again raised (42 mmHg by applanation tonometry). At this time the differential diagnosis included malignancy (melanoma, lymphoma, or leukaemia), granulomatous uveitis (sarcoidosis, tuberculosis, and coccidioidomycosis), and xantho-

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granuloma. An iris biopsy and aqueous humour cultures were recommended. The aqueous humour cultures were negative for bacteria and fungi.

On 11 May 1976 she underwent a filtering procedure, an iris biopsy superiorly, and a biopsy of the peripheral iris inferiorly. Both biopsies showed atypical melanocytes, forming plaques on the anterior iris surface and within the stroma. Delicate blood vessels within the surface plaques and rare chronic inflammatory cells also were noted (Fig. 1). The pathological diagnosis was malignant melanoma. One week after the glaucoma operation, with the patient on steroids and antibiotics, the eye remained quiescent with pressures ranging between 12 and 15 mmHg by applanation tonometry.

In June 1976 the patient's condition deteriorated, her visual acuity dropping from 6/24 to hand motion.

In spite of acetazolamide the intraocular pressure rose from 18 mmHg to over 40 mmHg. Keratic precipitates were noted on the corneal endothelium, and white flocculent material appeared on the anterior lens surface and in the inferior angle. Blood vessels extended into the whitish angle mass.

In July 1976 the patient complained of left orbital pain, nausea, and vomiting. Her visual acuity then was hand motion and her visual field was contracted. Her intraocular pressure was 40 mmHg, and the cornea was diffusely oedematous, with epithelial bedewing. The anterior chamber was deep. Severe flare and cellular reaction were noted, and a nodular mass filled the inferior angle. The pupil was non-reactive, dilated, and oval-shaped, with retraction of the iris at 12 and 6 o'clock. The anterior lens capsule was covered with flocculent debris; the

Fig. 1 Iris biopsy showing atypical melanocytes on iris surface (arrows) and in stroma. Microsection is through region of maximal tumour involvement (haematoxylin eosin, $\times 105$)

Fig. 2 Large calotte of enucleated eye showing white confluent nodules coating both the anterior iris and lens surfaces

Fig. 3 Tumour involvement of surgical wounds in vertically sectioned enucleated eye. (A) Level 1 shows the inferior iris biopsy wound (arrow) with extensive iris and ciliary body tumour. (B) Level 4 shows wound of filtering procedure (boxed area) and in (C) tumour infiltrating the superior wound ((A) Haematoxylin eosin, $\times 4$; (B) Haematoxylin eosin, $\times 4$; (C) Haematoxylin eosin, $\times 90$)

Fig. 4 Tumour cytological variations. (A) Tumour fills angle recess (triangle), ciliary body and iris stroma (asterisk), and both the trabecular meshwork and Schlemm's canal. (B) Tumour in stroma is virtually completely composed of spindle cells. (C) Epithelioid cells are preponderant in anterior chamber. (A) Haematoxylin eosin, $\times 320$; (B) Haematoxylin eosin, $\times 630$; (C) Haematoxylin eosin, $\times 630$

fundus could not be visualised. There was ciliary injection and conjunctival hyperaemia. Gonioscopy showed a small, nodular, tan mass extending throughout the inferior angle. The eye was enucleated on 22 July 1976.

PATHOLOGICAL FINDINGS

Macroscopic eye examination showed an irregular pupil with defects both superiorly and inferiorly, and

healing limbal wounds at 6 and 12 o'clock. On vertical sectioning nasal to the optic nerve there was a flocculent white 'exudate' partly filling the anterior chamber, coating the iris and lens, clogging the angles, and extending around an otherwise normal lens into the posterior chamber (Fig. 2). Anterior synechiae were noted at 11 o'clock. The optic disc showed a cup/disc ratio of 0.7. The vitreous was minimally hazy anteriorly but not invaded by tumour.

Microscopic examination showed both superior and inferior wounds, with a prominent iris mass inferiorly (Fig. 3). The tumour was minimally pigmented. Tumour cells were found in the trabecular meshwork around a few aqueous veins (Fig. 4), on the anterior lens surface, and in the anterior and posterior chambers. The iris stroma was primarily invaded by spindle-type melanoma cells, while the anterior chamber and its angle contained mainly epithelioid cells (Fig. 4). Occasional mononuclear inflammatory cells were found within the tumour. There was no extraocular extension, although both healing limbal wounds contained focal areas of tumour cells. The vitreous was free of tumour cells. The optic cup was markedly enlarged, and the lamina cribrosa was bowed posteriorly.

SUBSEQUENT CLINICAL FOLLOW-UP

In September 1976 an investigation for metastases was negative. In May 1977 (10 months after enucleation) a cyst-like lesion was noted along the conjunctival incision. Biopsy of this region revealed melanoma containing principally epithelioid-type cells (Fig. 5). Exenteration of the left orbit was advised but refused by the parents. In July 1977 (1 year after enucleation) a repeat investigation for

Fig. 5 *Conjunctival metastasis (12 months after enucleation), showing principally epithelioid cells (haematoxylin eosin, $\times 550$)*

Fig. 6 *Parotid gland metastasis (14 months after enucleation). Section shows parotid gland (on right) with adjacent lymph node containing metastatic melanoma, which is largely epithelioid (haematoxylin eosin, $\times 115$)*

metastases failed to reveal any evidence of distant spread. On 7 September 1977 (14 months after enucleation) an enlarged left preauricular lymph node was noted, the node being fixed to the underlying structures, not tender, and measuring 20 × 30 mm. The left upper anterior cervical lymph node was enlarged also. Two weeks later a left partial parotidectomy was done with left radical neck dissection. Wide excision of the conjunctiva overlying the orbital implant was also performed. Histopathological examination of the excised conjunctiva showed a small focus of tumour cells and lymphocytes, but the surgical margins were free of tumour. One lymph node in the partly excised parotid gland was heavily infiltrated by epithelioid tumour cells (Fig. 6). All cervical lymph nodes were free of malignant cells.

Discussion

The first description of tapioca melanoma was given by Reese *et al.* (1972), who used the term because of the clinical resemblance of the tumour to tapioca pudding. Subsequently this lesion has been reported only rarely (Jarrett *et al.*, 1966; Wilson *et al.*, 1976). On comparison with previously reported cases (Table 1), that reported here is unique mainly because of the presence of epithelioid-type cells and because of remote metastases.

Table 1 Clinical and pathological features of tapioca melanomas of the iris* compared with present case

	Previous cases*	Present case
Age (in years)	7, 21, 21, 21, 25, 27, 31, 34, 36, 38, 48	12
Sex: Female	6 of 11	Female
Male	5 of 11	—
Race	All white	White
Right eye	6 of 11	—
Left eye	5 of 11	1
Position†	7 of 11 inferior or infero-temporal quadrant	Inferior
No. of lesions	5 of 11 had 1 lesion 6 of 11 multicentric	— Multicentric
Shape	All nodular	Nodular
Pigmentation	8 of 11 little or none	Minimal
Cell type	All spindle	Epithelioid (predominant)
Ocular tension	Elevated in 4 of 11	Elevated

* Eleven total previously reported cases. † Position of largest or only nodule

Table 2 Clinical management and survival of patients with tapioca melanoma of the iris

Procedure	Number of patients	Follow-up period (s)*
Preliminary iridectomy followed by enucleation	1‡, 3§	11 years, 11 years, 8 years (no follow-up on 1)
Enucleation only	1§	15 months
Iridectomy only	3§	19 months, 8 months, 6 years
Iridocyclectomy and photocoagulation	1	5 years
Iridectomy followed by enucleation and by lymph node dissection	1†	14 months
No surgical procedures	2§	No follow-up

* All patients have no recurrences and no evidence of metastasis.

† Present case. ‡ Jarrett *et al.* (1966). § Reese *et al.* (1972). || Wilson *et al.* (1976)

Few iris melanomas contained epithelioid-type cells (Richardson, 1948; Cleasby, 1958; Ashton, 1964; Roy, 1967), whereas all previously reported tapioca iris melanomas contained spindle-type cells (Jarrett *et al.*, 1966; Reese *et al.*, 1972; Wilson *et al.*, 1976). Tapioca iris melanomas were always nodular and multicentric, most often inferior, and in some patients associated with a raised intraocular pressure. Although their surgical management differed and one-half underwent enucleation, all had a favourable outcome (Table 2). Follow-ups of 2 months to 11 years in those patients who had a surgical intervention revealed no local recurrence, and none of the remainder were complicated by metastases. Thus it is likely that both the epithelioid cell predominance and the biological aggressiveness of this neoplasm contributed to the systemic metastases. Finally, it should be stressed that the diagnosis of malignant iris melanoma should always be entertained in cases of unilateral iritis or glaucoma that are resistant to conventional treatment. The present patient is alive and free of detectable tumour metastases 14 months after invasion of lymph nodes and 28 months after enucleation.

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