Intraocular melanoma, diabetes, and Turner's syndrome: presentation with proptosis

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SUMMARY A patient with Turner's syndrome and untreated diabetes mellitus presented with a blind, painful, glaucomatous eye and progressive unilateral proptosis. Although a computerised tomographic scan failed to show evidence of a retroocular extension of the presumed choroidal melanoma, the clinical features were so suggestive of extraocular extension that an orbital exenteration was considered. Examination of the enucleated eye for histological confirmation of the presence of malignant melanoma showed no extraocular extension, and histology of the retroocular connective tissue revealed only haemorrhage and fibroblastic activity. There are 3 other reported cases of malignant melanoma presenting as proptosis without extraocular extension, so that extreme caution is required when exenteration is deemed necessary on clinical grounds but where computerised scanning fails to reveal direct tumour spread.

Case report

A 32-year-old female presented in November 1979 with a 2-day history of nausea, vomiting, decreased vision, and dull pain around the right eye. She denied any previous ocular symptoms, though her mother had noticed intermittent redness of the eye over the previous 6 months.

She was known to have Turner's syndrome (45X/46XX), and developed diabetes mellitus 11 years ago. Other than keeping to a relatively sugar-free diet she had refused treatment for her diabetes mellitus. Her paternal grandfather had also been diabetic.

EXAMINATION

The patient was frightened, withdrawn, and denied having symptoms. She was short in stature and lacked any secondary sexual characteristics as expected in Turner's syndrome, but there was no hepatosplenomegaly or lymphadenopathy.

The right upper lid was markedly swollen, there was chemosis of the right eye (Fig. 1), and there was a grey-brown swelling just behind the superior limbus suggesting an underlying mass. There was 4 mm of right proptosis, and movements of the right eye were restricted in all directions.

The right cornea was oedematous. The anterior chamber was absent inferiorly where the iris was dis-

placed forward and on which there was a large abnormal blood vessel. The upper part of the anterior chamber was filled with a fibrinous blood clot and the intraocular pressure was 35 mmHg. There was no red reflex on transillumination, and there was doubtful light perception with loss of consensual pupil response.

Except for a few macular drusen, the left eye was normal.

Laboratory investigation confirmed the untreated diabetes, with a random blood glucose of 18 mmol/l (normal range 3.0-5.5). Haemoglobin was 16.5 g/dl,

Fig. 1 Right eye of patient 2 days after admission showing proptosis and extreme chemosis.

Fig. 2 Computerised axial tomography showing proptosis and thickening of posterior coats of the eye but no discrete extraocular mass.

and the white cell count was $15\,500 \times 10^9/l$ with a neutrophilia.

Examination of the nasopharynx did not show any mycotic infection or gross abnormality. B-scan ultrasonography of the right eye showed it to be full of immobile echoes, densest superotemporally in the ciliary body region, with generalised thickening of the eye wall posteriorly and temporally.

Computerised axial tomography (CT) scanning of the orbits (Fig. 2) demonstrated enlargement of the right globe and thickening of its coats, especially posterolaterally. However, no retroocular mass was seen.

Skeletal radiological survey and hepatic colloid scintigraphy did not show any metastases. Urinary melanogens were not detected.

Fig. 3 Enucleated eye showing tumour on temporal side of anterior choroid. (Haematoxylin and eosin, $\times 2.8$).

The subsequent clinical course was one of increasing lid swelling and conjunctival chemosis, with proptosis, which progressed from 4 to 8 mm over the succeeding 4 days.

Her clinical signs suggested a choroidal malignant melanoma with extraocular, including retrobulbar, spread, despite the contrary evidence of CT scanning, and a lid-sparing orbital exenteration was considered. Because of the lack of radiological evidence of a retrobulbar mass a 'blind' needle biopsy of the orbit would not have been satisfactory and was not carried out. Instead the visible upper scleral discolouration was exposed surgically with the intention of carrying out a biopsy. When this was found to be a staphyloma, instead of biopsy enucleation was performed. There was no macroscopic evidence of extraocular tumour. Biopsies were taken from the retrobulbar soft tissue.

Within the follow-up period of 10 months there has been no sign of local tumour recurrence.

HISTOPATHOLOGICAL REPORT

A large necrotic malignant melanoma was present (Fig. 3), with its apparent origin in the temporal anterior choroid, which was pressing the funnelled detached retina towards the nasal side. Many intraocular structures were necrotic (Figs. 4, 5), the tumour having very few apparently viable cells (Fig. 6). The lens contained blood within its capsule and was surrounded by exudate, haemorrhage, and by tumour posteriorly. The iris showed marked fibroblastic activity. The choroid was the seat of an intense inflammatory reaction with necrosis, indicating a panophthalmitis, which is probably aseptic. Parts of the choroid also contained fibroblastic activity with a marked reaction of the vascular endothelium, showing congestion and haemorrhages. Similar changes were found in the scleral channels and in the episclera. The activity of fibroblasts was such that some had taken on pseudoneoplastic appearances. Only one clear tumour deposit could be demonstrated in a scleral channel, but other clusters could have been concealed by the intense activity due to reactive changes from necrosis and inflammation.

Discussion

This case presented a number of problems in management. Firstly, the patient was an extremely unreliable witness and no credence could be placed on the history to give an accurate picture of her symptoms and their duration. There was a possibility that there was no tumour and her ocular and orbital haemorrhage was caused by trauma or infection, the likelihood being increased in a patient with untreated diabetes.

However, no evidence was found to suggest either

Fig. 4 *Recognisable but partly necrotic ciliary process on one side of tumour. (H and E, $\times 14$).*

a bacterial or fungal infection either preoperatively or from the tissues taken from the retrobulbar space at operation.

Secondly, if a tumour was present, in the absence of other pathology the signs of acute orbital cellulitis could mean extraocular spread, especially in view of the rapidly increasing proptosis. If an extraocular spread was assumed, the question of an exenteration arises. While CT scan of this case did not show a discrete retrobulbar mass, there was thickening of the wall of the globe, and there was still a possibility that

spread of a tumour had mostly been confined to the plane of the sclera. In the event our more conservative approach of enucleation was justified.

Ocular inflammation as the presenting feature of malignant melanoma is well documented. Fraser and Font¹ reviewed 450 eyes enucleated for malignant melanoma and listed 22 patients with choroidal or ciliary body malignant melanoma which presented initially with ocular inflammation, 8 of them as panophthalmitis. They also listed 13 patients who presented with intraocular haemorrhage as the initial

Fig. 5 *Part of the choroidal 'foot' of melanoma and part of 'head of mushroom', both showing necrosis. (H and E, $\times 14$).*

Table 1 Review of reported cases of choroidal melanoma with panophthalmitis and proptosis

Author	Case no.	Sex, Age	Extraocular and inflammatory signs	Tumour extension
Reese <i>et al.</i> ²	2	F, 23	Lid oedema, chemosis, proptosis	None
Reese <i>et al.</i> ²	5	F, 58	'Swelling, inflammation', proptosis	To orbital bones and sinuses
Reese <i>et al.</i> ²	7	F, 48	Lid swelling, chemosis, 'exophthalmos'	To orbit
Reese <i>et al.</i> ²	13	M, 69	Hypopyon, proptosis, globe immobility	To orbit and sinuses
Kline <i>et al.</i> ⁵		M, 63	Lid oedema, chemosis, proptosis 11 mm	None
Fraser and Font ¹	3	M, 66	'Orbital cellulitis', proptosis	None
Zimmerman and McLean ⁴	29	M, 58	Hypopyon, orbital inflammation, proptosis	Posterior epibulbar nodule
Buckley and Cheng		F, 32	Hypopyon, hyphaema, lid oedema, chemosis, proptosis 8 mm, globe immobility	None

sign. In only 1 of their patients was proptosis a significant feature and extensive necrosis was thought to be the cause of the acute panophthalmitis.

Reese *et al.*² reviewed cases of malignant melanoma presenting with signs of inflammation and described 2 groups according to whether there was 'mild necrosis' in the tumour which generally had mild inflammation, or 'coagulation necrosis' which was associated with more severe inflammation. In the latter group he described 17 patients presenting with more marked inflammation and 4 of these patients also had proptosis. The pathology of this group was characterised by massive necrosis of tumour tissue and formation of cystic spaces. Two of the 4 cases had extraocular spread into adjacent bony structures.

In a later publication Reese³ described 6 cases of malignant melanoma of the choroid which underwent necrosis and presented with signs of panophthalmitis and proptosis; all had extraocular extension. Zimmerman and McLean⁴ in reviewing a number of

untreated malignant melanomas with metastases also reported a case of proptosis associated with orbital inflammation, hypopyon, and uveitis, but their case also had a posteriorly placed epibulbar nodule which was evidently a local extension. Only Kline *et al.*⁵ reported a similar case of intraocular haemorrhage, panophthalmitis, and severe proptosis (11 mm) without extraocular spread, but this case was complicated by having been hit by a bottle above the affected eye 12 hours previously.

It would seem that, while ocular inflammation, haemorrhage, and panophthalmitis may occur as an uncommon way of presentation of uveal malignant melanoma, proptosis is more often associated with extraocular spread but may rarely be a prominent feature of a necrotic uveal malignant melanoma without any spread of the growth outside the globe (Table 1). The mechanism of acute panophthalmitis and orbital cellulitis is not known but is probably associated with thrombophlebitis and occlusive vasculitis, which may have an autoimmune basis as postulated by Reese.³

From the clinical point of view, when a malignant melanoma gives rise to panophthalmitis and proptosis a CT scan may distinguish between cases with and without extraocular spread. If no retrobulbar mass is demonstrated, enucleation with biopsy of orbital contents and not exenteration should be the operation of choice.

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References

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Fig. 6 Necrotic central mass. (H and E, $\times 382$).