# The eye in malignant disease

*Chun H Lau, Simon Taylor*

## INTRODUCTION

The eye and its adnexae (the extraocular muscles, orbit, orbital walls and eyelids) can be involved in malignant disease, either as the primary source of the tumour or as a site of secondary metastatic involvement. Indeed, there is a wide variety of different tumours which are known to affect the eye, this diversity being a consequence of the richness of the ocular tissues present. In addition, disorders of vision or eye movements may be the presenting signs and symptoms of intracranial malignancy.

The occurrence and frequency of tumours differs with age; for example retinoblastoma is an important childhood tumour, whereas basal cell carcinomas are much more common in the elderly.

Management of ocular malignancy is often difficult, and requires a multidisciplinary approach aimed at preserving life and, if possible, vision. Considerations therefore range from choosing the most effective treatment modalities to maintaining ocular comfort and cosmesis.

## PRIMARY OCULAR MALIGNANCIES

Primary intraocular and extraocular malignancies can present de novo with symptoms and signs of either local spread or distant metastases. All ocular tissue components are known to produce malignancies and have been extensively reviewed (Char, 1989). Affected tissues include: neural, vascular and muscle tissues; sebaceous, sweat and lacrimal glands; fibrocytes; osteocytes; epithelium; melanocytes; photoreceptor cells; leukocytes; lymphoid tissue.

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Local spread of primary tumours can involve the adjacent skin, orbital contents, orbital wall or cranium by direct extension or progression through local foramina and fissures as well as bone invasion and erosion.

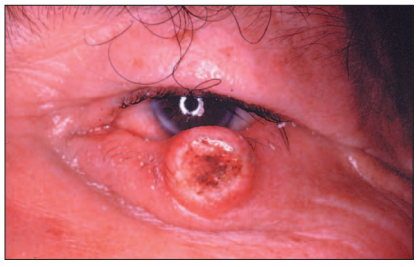
### Primary malignancies of the external eye

Primary tumours of the eyelids and periocular skin are much more common than those of the lacrimal tissues or conjunctiva. The principal types are basal cell carcinomas (*Figure 1*) and squamous cell carcinomas, which together account for about 99% of all eyelid malignancies.

Basal cell carcinomas are the most common ocular adnexal malignancy and are much more common in Caucasians. They typically present from the sixth decade onwards and account for 90% of all eyelid cancers (Aurora and Blodi, 1970). They spread locally and rarely metastasize. The lower lid is most frequently involved, being affected in over 50% of cases, followed by the medial canthal region, the upper lid and, least commonly, the lateral canthal region (Milvertson, 1977). The most important precipitating factor for the development of basal cell carcinomas is ultraviolet radiation; other factors include previous radiotherapy exposure and acquired immunodeficiency syndrome (AIDS).

Squamous cell carcinomas account for about 9% of eyelid malignancies (Reifler and Hornblass, 1986), but are more serious as they have a higher rate of metastasis. They also usually occur after the sixth decade, although they are not unknown in young adults with albinism, xeroderma pigmentosum or who are immunosuppressed. They also affect the lower lid more frequently. It is the keratin production which causes the characteristic surface crusting.

*Figure 1. Basal cell carcinoma involving the eyelids and periocular skin.*

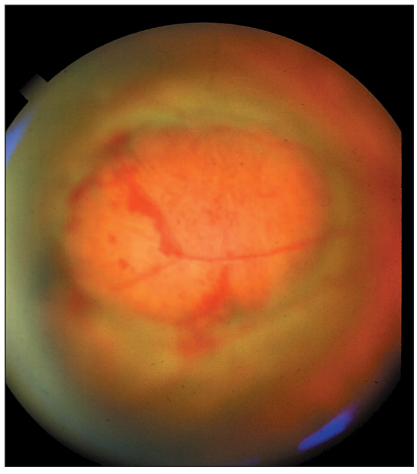


### Primary intraocular malignancies

Uveal melanomas are the commonest adult intraocular malignancy, the uvea being the pigmented layer of the eye that comprises the iris, ciliary body and choroid. Choroidal melanomas (*Figures 2* and *3*) are the most common, with an incidence of about 5–7 per million per year (Char, 1978), and have a predilection for Caucasians over pigmented races. Melanomas of the ciliary body and iris are less common, the relative incidence of choroid:ciliary body:iris involvement being 20:6:1. Uveal melanomas metastasize readily to the liver, skin (as subcutaneous nodules), vertebrae, lung and CNS.

Retinoblastomas (*Figures 4* and *5*) are tumours unique to the eye which arise from primitive photoreceptor cells and comprise the commonest childhood

*Figure 2. Fundus picture showing choroidal melanoma (grey mass) with growth from choroid through Bruch's membrane to subretinal space (yellow mass with associated haemorrhages. Bright yellowness secondary to fluorescein angiography).*



intraocular malignancy. They occur in about 1/20 000 live births and 90% present before the age of 3 years, typically with leukocoria (a white pupil) or a squint. Bilateral involvement occurs in 40% and usually presents earlier than unilateral cases. These are aggressive tumours that spread locally to the orbit, as well as metastasizing to the CNS, liver and kidneys (MacKay et al, 1984). As there is a hereditary element, future siblings and offspring of affected individuals are screened.

Large cell non-Hodgkin's lymphoma can affect the eye with multiple manifestations (Freeman et al, 1987) including chronic diffuse uveitis. Ocular involvement most commonly occurs in ocular and ocular–CNS lymphoma (75% of cases), but can occur through metastasis in systemic lymphoma (25% of cases). Hodgkin's lymphoma can also cause ocular metastases (Towler et al, 1999).

*Figure 3. Ultrasound image showing intraocular mass (choroidal melanoma) with associated serous retinal detachment.*

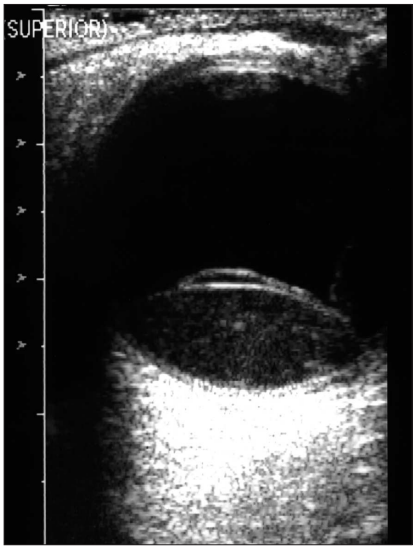



*Figure 4. Fundus picture showing retinoblastoma.*

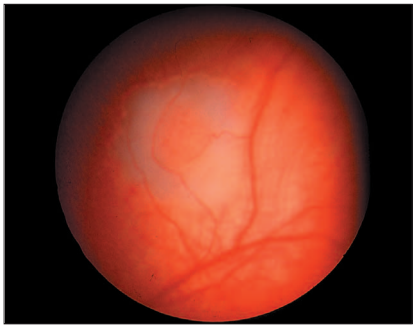
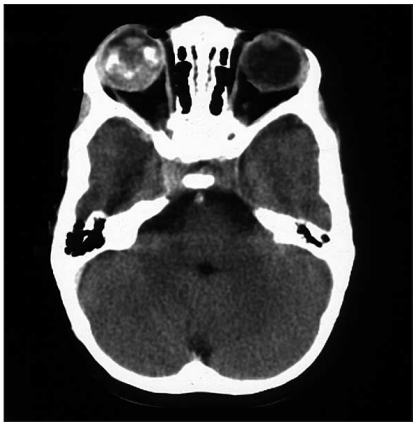


*Figure 5. Computed tomogram showing right intraocular retinoblastoma with foci of calcification.*

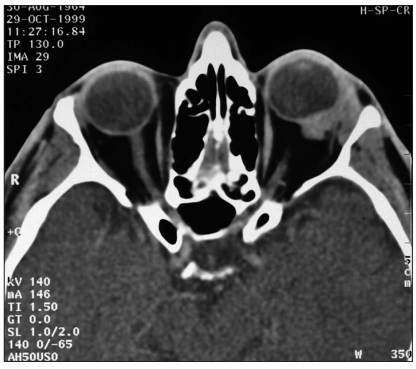


### Primary orbital malignancies

Orbital malignancies usually present with the gradual onset of unilateral proptosis owing to volume expansion within a confined space. This can lead to pain, visual changes, local oedema, and deformity, especially around the eyelids. Eccentric deviation of the globe (*Figure 6*) suggests extraconal lesions (i.e. outside the cone formed by the four recti muscles) while axial proptosis suggests an intraconal lesion.

Although orbital tumours occur far less frequently in children, rapid onset of proptosis should raise the suspicion of a rhabdomyosarcoma or neuroblastoma (Musarella et al, 1984). Rhabdomyosarcoma is the commonest childhood orbital malignancy and arises from undifferentiated mesenchymal cells. It is more common in Caucasian boys and accounts for 5% of childhood cancers (Miser and Pizzo, 1985).

*Figure 6. Computed tomogram showing left orbital melanoma with nonaxial proptosis.*




The most common adult optic nerve tumour is an optic nerve sheath meningioma, which typically presents in middle-aged women with gradual visual loss. The intraorbital type is about three times more frequent than the intracanalicular type (Macmichael and Cullen, 1969; Karp et al, 1974).

Lymphomas (*Figure 7*) should not be forgotten when considering the causes of orbital malignancies and can be found anywhere within the orbit; additionally, they occur bilaterally in 18% (McNally et al, 1987).

## SECONDARY OCULAR MALIGNANCIES

Ocular metastases are common and derive from tumours of the breast, lung, kidney, gastrointestinal and genitourinary systems. Metastases can involve the eye (in particular the choroids (*Figure 8*) owing to their extensive blood supply) or the adnexae; in adults, intraocular metastases are much more common than orbital metastases. In about 30% of orbital metastases from

*Figure 7. Computed tomogram showing left orbital intraconal lymphoma with axial proptosis.*

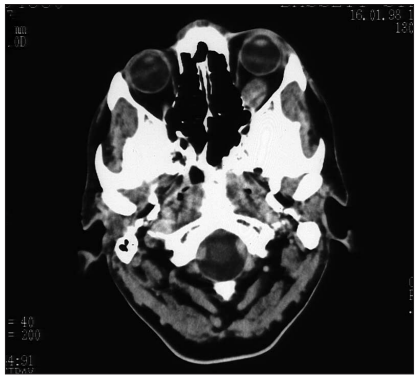
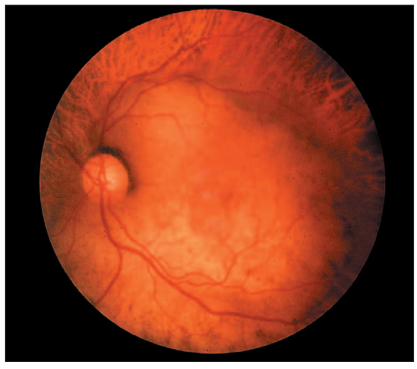


*Figure 8. Fundus picture showing choroidal secondary tumour from breast carcinoma.*



distant primaries, the orbital presentation precedes that of the primary, the most common primary being breast cancer (Shields et al, 1988).

Neuroblastomas arise from sympathetic ganglion tissue and account for 7% of childhood malignancies (Lopez-Ibor and Schwartz, 1985). They comprise the commonest childhood secondary orbital tumour. In leukaemia, intraocular involvement is common but mostly sub-clinical.

Ocular secondary tumours can also derive from local extension of primaries within the cranium (e.g. intracranial meningioma), orbital walls (e.g. osteogenic sarcoma, plasmacytoma), paranasal sinuses (e.g. squamous cell carcinoma, adenoid cystic carcinoma) or the nasal tract.

## CNS MALIGNANCIES WHICH AFFECT VISION OR OCULAR MOTILITY

Many areas of the CNS are involved in ocular function. Depending on the size and location of CNS lesions, the visual pathways or cortical and sub-cortical oculomotor systems can be affected resulting in visual loss, visual field defects (e.g. bitemporal hemianopia), endocrine disorders (hypothalamus or pituitary lesions), pupil reflex abnormalities, diplopia and paralysis of eye or eyelid muscle movements.

In adults, metastatic brain tumours are more common than primary malignancies (glioma being the commonest of the primaries) and may simultaneously involve several different areas of the brain. The extra tissue volume produced by brain malignancies or the associated obstruction to CSF outflow and drainage through the ventricles result in increased intracranial pressure and associated papilloedema with or without obstructive hydrocephalus.

## OCULAR COMPLICATIONS OF MALIGNANCY TREATMENT

Ocular complications can also result from tissues damaged by treatment: corticosteroids are known to induce cataracts and secondary glaucoma; chemotherapy may lead to opportunistic infections (e.g. cytomegalovirus, herpes zoster virus); radiation therapy can induce dry eye, cataract and radiation retinopathy.

## MANAGEMENT

The principles of malignancy management in relation to the eye are:

1. Early diagnosis from the medical history, a neurological and ophthalmic examination, and the help of appropriate imaging including ultrasound, X-ray, computed tomography and magnetic resonance imaging
2. Confirmation of diagnosis by tissue biopsy
3. Treatment options:
   a. Removal of as much of the tumour as possible, maintaining visual function if possible, by excision, enucleation or exenteration
   b. Radiotherapy and/or chemotherapy for non-resectable tumours
   c. Other treatment modalities, including cryotherapy for eyelid tumours and laser photocoagulation or ablation for intraocular tumours
4. Rehabilitation with cosmetic reconstructive procedures
5. Long-term follow up to manage disease, detect recurrence and manage late complications of treatment (*Table 1*).

## CONCLUSIONS

Prognosis is variable and depends on tumour type, extent, size, location, the presence or absence of metastases, the response to therapy, the patient's age and general health. The management team is usually multidisciplinary and includes ophthalmologists, paediatricians, oncologists, physicians, neurologists, neurosurgeons, radiologists, radiotherapists, plastic surgeons and prosthetics experts. HM

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**TABLE 1.**
**Ocular complications secondary to treatment for malignancies**

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| Depigmentation, loss of eyelashes (lid cryotherapy) |
| Extraocular muscle fibrosis and cranial nerve palsies |
| Lid defects and malposition from tissue loss |
| Dry eye from lacrimal gland, ducts damage, or lid malposition |
| Watering eye from lacrimal drainage apparatus damage, lid malposition |
| Ocular surface disorder from cicatricial changes to conjunctiva and cornea |
| Secondary glaucoma from aqueous drainage apparatus damage |
| Cataract from radiation or corticosteroid treatment |
| Retinopathy, optic neuropathy (radiation induced or toxicity from chemotherapy) |
| Opportunistic infection and secondary malignancy induced by radiotherapy or chemotherapy |