# Choroidal melanoma

The uveal tract is the highly vascular and densely pigmented layer of the eyeball, lying between the sclera (superficial to it) and the retina (deep to it). The anterior, visible portion is the iris. This extends back into the ciliary body (at the level of the lens) and then extends around to the posterior pole. It is this fundus portion which is known as the choroid.

See also Anatomy of the eye for diagram and further information.

## Pathogenesis

Primary choroidal melanoma arises from melanocytes within the choroid. It is thought to develop from pre-existing melanocytic naevi, although de novo growth may occur. The colour varies from darkly pigmented to amelanotic. It is usually dome-shaped.

If it breaks through Bruch's membrane (which effectively forms a blood/neural tissue barrier between the vascular choroid and the retinal layer) as it grows, it looks like a mushroom. It can also be bilobular, multilobular and diffuse in shape. Occasionally, there may be a number of small lesions in one or both eyes (although bilateral involvement is rare).

Histologically, three distinct cell types are recognised: spindle A, spindle B and epithelioid. The latter is associated with more aggressive disease and increased metastatic potential. These types of tumours tend to have a worse prognosis.

## How common is choroidal melanoma? (Epidemiology)

- Uveal melanoma is the most common primary intraocular tumour in adults with a mean age-adjusted incidence of 5.1 cases per million per year. Tumours are located either in iris (4%), ciliary body (6%), or choroid (90%).[1]

- Up to 50% of patients develop metastatic disease. Metastases are most frequently localised to the liver and, as few patients are candidates for potentially curative surgery, this is associated with a poor prognosis.[2]
- While the disease has no gender preference it is more common in middle-aged Caucasians with a median age of presentation of 58 years.[3]
- 98% of cases occur in Caucasians.[4]

### Risk factors[3]

- Light-coloured irides.
- Possibly sunlight exposure.
- Positive family history (although frequently absent).
- Pre-existing naevus.
- Congenital ocular melanocytosis.
- Xeroderma pigmentosum.

## Choroidal melanoma symptoms (presentation)[3]

- Mostly presents with painless loss or distortion of vision (metamorphopsia).
- Larger tumours are associated with a serous (fluid) retinal detachment causing flashing or flickering of light (photopsia).
- In some cases, the person is entirely asymptomatic, with the tumour identified on routine ophthalmic screening.
- When the anterior segment of the eye is affected, presentation may be discolouration of the iris or persistent injection of the episclera, or chronic conjunctivitis.
- Ciliary body tumours can cause increased and asymmetric astigmatism due to displacement of the intraocular lens.
- Rarely, a blind eye or one with a dense cataract may harbour an occult melanoma.

The tumour may have metastasised before ocular symptoms occur and a diagnosis is made. Additionally, metastases from primary non-ocular malignancy can give rise to a secondary tumour in the eye. Therefore, there may be a history of weight loss, fatigue, cough or change in bowel or bladder habits suggestive of systemic involvement.

## Differential diagnosis

Patients with suspicious pigmented lesions should be assessed by an ophthalmologist with clinical expertise in ocular tumours. Diagnostically small melanomas need to be differentiated from benign naevi. The clinical appearance and ophthalmoscopic features assist with this differential:[3]

- The presence of subretinal fluid, orange pigment and documented growth on fundus photography are findings that support the diagnosis of melanoma.
- Drusen and pigment epithelial changes are more suggestive of a benign lesion.

Depending on clinical presentation, the differential diagnoses may include:

- Naevus.
- Melanocytoma.
- Metastasis from a non-ocular tumour.
- Choroidal detachment.
- Intra-ocular foreign body.
- Cavernous haemangioma.
- Exudative retinal detachment (of other cause).
- Wet age-related macular degeneration.
- Retinoblastoma (particularly in a young patient).
- Glaucoma.
- Sarcoidosis.
- Tuberculosis.

## Investigations[3]

Ultrasound (US) imaging can be used to help establish the diagnosis, evaluate possible extra-ocular extension, estimate tumour size for periodic observation and to plan treatment. Sequential scans are important for cases of diagnostic uncertainty.

CT scan and MRI of the globe and orbit are more expensive than US and less sensitive, although they may be helpful in assessing extra-ocular extension.

US scanning must be followed up by further investigations to ascertain whether this has spread or has arisen as a result of spread. These include LFTs, particularly alkaline phosphatase, glutamic-oxaloacetic transaminase, lactic dehydrogenase and gamma-glutamyl transpeptidase. If these are abnormal, imaging of the liver is mandatory; the liver is affected in up to 90% of patients with metastases.[5]

In some instances, a diagnostic biopsy may be indicated, particularly when the lesion is amelanotic or difficult to assess due to vitreous haemorrhage or debris.

Diagnostic biopsy must be distinguished from prognostic biopsy (where the tumour is assessed for genetics and risk of future metastasis).

Fine needle aspiration can be performed but requires the assistance of a skilled cytologist familiar with ocular pathology.

## Staging

Choroidal melanomas are staged according to the T (tumour) N (lymph node involvement) M (metastases) system.[6]

## Choroidal melanoma treatment and management[7]

There are several ways to manage choroidal melanomas. Factors to take into account include:[8]

- Visual acuity of the affected eye.

- Visual acuity of the contralateral eye.
- Size of the tumour.
- Age and general health of the patient.
- Ocular structures involved.
- Presence of metastases.
- Patient's wishes.

Choice of treatment of choroidal melanoma remains controversial. Although enucleation has been the treatment of choice in the past, research has shown that vision-sparing approaches might offer similar degrees of tumour control. A multicentre randomised trial by the Collaborative Ocular Melanoma Study (COMS) Group showed that patient survival after treatment with plaque radiotherapy is similar to enucleation for medium-sized melanoma.[9]

### Non-surgical

- Observation may be acceptable for posterior uveal tumours where diagnosis is not well established. In particular, tumours of <2-2.5 mm in elevation and <10 mm in diameter can be observed until growth is documented.[10]
- Laser photocoagulation and transpupillary thermotherapy are used in selected small choroidal melanomas. The latter may be a stand-alone treatment for flat tumours or given in combination with plaque radiotherapy for thicker tumours. Melanomas selected for laser treatment tend to be smaller and visibly accessible, which means these tumours are usually located in the posterior choroid.[11]
- However, thermotherapy and photodynamic therapy do not offer local tumour control rates that are equivalent or higher than those achieved with plaque or proton radiation therapy.[12]
- Stereotactic radiosurgery may provide good local tumour control.[13]
- More than 90% of patients treated with eye-preservation options receive some form of radiotherapy.[14] Two of the most widely used forms of radiation therapy are iodine-125 and ruthenium-106 brachytherapy.[15]

- External beam irradiation using charged particles, either protons or helium ions, is a frequently used alternative method to treat medium-sized choroidal melanomas (<10 mm in height and <15 mm in diameter), although it has been used for larger tumours. It has similar indications and success rates to plaque brachytherapy.[16]

### Surgical

- Block excision, or sclerouvectomy, is an alternative treatment method for choroidal melanomas. It is reserved for small tumours covering less than one third of the globe's circumference.
- Plaque brachytherapy is a widely accepted alternative to enucleation.[17] [18]
- Enucleation is the classic approach to choroidal melanomas and has been the preferred treatment for large and complicated tumours, which compromise visual function and where other therapies tend to fail. It is also advocated in severely sight-impaired, painful eyes with melanoma-induced neovascular glaucoma.
- Orbital exenteration is a radical treatment reserved for cases with widespread orbital extension. Patients with such advanced melanomas are likely to have extensive distant metastases and poor prognosis for survival, with or without orbital exenteration surgery.

### Metastatic disease

In cases where distant metastases are found at first presentation, management of the intra-ocular melanomas becomes palliative. Systemic chemotherapy is the primary treatment at that point. See also the separate article on Malignant Melanoma.

Various therapies for metastatic disease have been reported. Treatment may include supportive care, systemic therapies (chemotherapy, biological therapies) or liver-directed therapies (chemotherapy, radiotherapy or surgery). Systemic chemotherapy results in an objective response rate that ranges from 5% to 15% and without any strong evidence that conventional chemotherapy prolongs survival.[19]

## Complications

The most important complication of this tumour is metastasis. However, a number of ocular problems may occur in the early stages, including:

- Retinal detachment.
- Choroidal neovascularisation.
- Haemorrhage.
- Uveitis.

Occasionally, the tumour may spread anteriorly, thus affecting segments at the front of the eye and so resulting in cataract formation, ocular hypertension/hypotension or iris rubeosis. Treatment of the tumour may also lead to partial or total loss of vision in the eye.

## Prognosis[20]

The prognosis depends mostly on the genetic alterations and tumour size. Every millimetre increase in thickness leads to a 5% increased risk for metastasis.[4]

Median survival after liver metastasis is poor (4-6 months). One-year survival is 10-15%.[7]

Other features associated with an increased risk of mortality include:

- Anterior location.
- Trans-scleral extension.
- Optic nerve extension.
- Lack of pigmentation.
- Certain histological characteristics.

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## Further reading

- Choroidal Tumours; Eye Cancer Network

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