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.

Uveal melanoma is a serious life-threatening intraocular malignancy, primarily involving the choroid (90%), ciliary body (7%) or iris (2%).[1]

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 generally 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.

Uveal melanoma is the most common primary malignant intraocular tumour in adults. The 10-year cumulative metastatic rate is about 34%. The most common site of metastasis is the liver (95%).[2, 3]

Less frequently, choroidal melanoma can metastasise locally into the orbit, the conjunctiva or the maxillofacial bones.[4]

Epidemiology

- 98% of cases occur in Caucasians.[1]
- It is rarely found among black people. Those of Hispanic and Asian origin are thought to have a small risk compared with white people.
- There is a slightly higher incidence in men for all age groups, except from 20-39 years, when a small predilection exists for women.
- Incidence peaks at around 55 years of age.

Risk factors

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

The tumour growth tends to be asymptomatic. In general, the further the tumour is away from the optic nerve and fovea, the less likely it is to produce symptoms. Therefore, it may be found incidentally during ophthalmoscopy. If it reaches a certain size or is in a sensitive location it causes visual disturbance and other ocular symptoms.

Ocular symptoms
- Blurred vision.
- A paracentral scotoma.
- Painless and progressive visual field loss.
- Floaters or flashes (‘ball of light’ slowly moving across vision).
- Occasionally severe ocular pain.

Systemic symptoms
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.

Signs
- Loss of visual acuity ± visual field defects.
- Occasional inflammation (marked by inflammatory cells in the vitreous).
- Usually: nodular, dome-shaped lesion on fundoscopy; occasionally: diffuse lesion growing laterally.
- Varying colours but may be amelanotic (difficult to pick up).[6]
- Occasionally: haemorrhage or hyphaema.
- May be ‘hidden’ under a large retinal detachment.
- Advanced tumours may give rise to proptosis.

Differential diagnosis
- 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
Ultrasound (US) imaging can be easily carried out in the outpatient department and 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]

Fine-needle aspiration biopsy is the current standard of care for assessing prognosis because of increasing molecular knowledge about choroidal melanomas.[6]

Staging
Choroidal melanomas are staged according to the T (tumour) N (lymph node involvement) M (metastases) system.[7]

Management[2]
There are several ways to manage choroidal melanomas. Factors to take into account include:

- 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.

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. [8]

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. [9]
• 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.
• 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. [10]
• Stereotactic radiosurgery may provide good local tumour control. [11]
• More than 90% of patients treated with eye-preservation options receive some form of radiotherapy. [12] Two of the most widely used forms of radiation therapy are iodine-125 and ruthenium-106 brachytherapy. [13]
• 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. [14]

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. [15, 16]
• 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. [17]

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 [18]
The prognosis depends mostly on the genetic alterations and tumour size. Every millimetre increase in thickness leads to a 5% increased risk for metastasis. [1]

Median survival after liver metastasis is poor (4-6 months). One-year survival is 10-15%. [2]

Other features associated with an increased risk of mortality include:

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

Further reading & references

- **Choroidal Tumours; Eye Cancer Network**

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**Peer Reviewer:**
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**Document ID:**
4059 (v23)

**Last Checked:**
18/08/2015

**Next Review:**
16/08/2020

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