

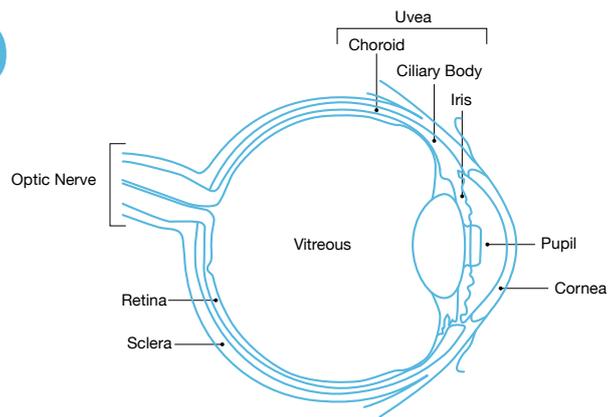
Ocular Melanoma

Primary Cancer



Introduction

Ocular melanoma includes two types of cancers: one that develops within the eye (also known as uveal melanoma) and one that can develop on the surface of the eye, conjunctival melanoma. Uveal melanoma arises from structures in the middle layer of the eye – that is, from the iris, choroid or ciliary body. There are approximately 600 new cases of uveal melanoma in the UK each year. Conjunctival melanoma is very rare, representing only 1–2% of all ocular melanomas with only 15–20 patients each year developing this in the UK. In this leaflet we concentrate on uveal melanoma.



Symptoms & Signs of Uveal Melanoma

Mnemonic devised by Bertil Damato

M Melanoma visible externally, as extraocular extension, an iris tumour, or iris heterochromia (discolouration)

E Eccentric visual phenomena, such as field loss and photopsia, caused by a tumour or secondary retinal detachment

L Lens abnormalities such as astigmatism (causing blurring / distorted vision) and cataract, caused by a ciliary body tumour

A Afferent pupillary defect, caused by tumour or retinal detachment

N No optical correction, because of blurring or metamorphopsia (straight lines look wavy) from macular oedema, retinal detachment or tumour

O Ocular hypertension from rubeosis iridis or tumour cells or macrophages in angle

M Melanosis oculi (naevus of Ota ; black-bluish skin and scleral pigmentation)

A Asymmetrical episcleral vessels, indicating a ciliary body tumour

Referrals

Uveal melanomas are often discovered via routine optometrist eye examination. Sometimes the patient will present with symptoms, such as flashes of light, blurry vision, loss of vision, floaters etc. On discovering or suspecting a tumour, optometrists or GPs should immediately refer directly to the local ophthalmology department, usually through an emergency eye clinic.

If an ophthalmologist suspects uveal melanoma, they must make a referral within 48 hours to one of four supra-regional centres; Glasgow (Tennent Institute), Liverpool (RLBUHT), London (St Barts and the London), Sheffield (Hallamshire). Patients must be seen within 2 weeks.

Treatments

The four supra-regional centres offer a variety of treatments for gaining local control over uveal melanomas, including radiotherapy (plaque or proton beam radiotherapy, and stereotactic radiosurgery), phototherapy (transpupillary thermotherapy and photodynamic therapy) and surgery (local resection, endoresection and enucleation).

The treatment chosen will depend on the location and size of the tumour. For example, a very large uveal melanoma will usually require enucleation. The aim of treatment is to prevent metastases, conserve vision and avoid pain.

Tumours that regrow after treatment, or those that extend outside of the eye, are associated with a poor prognosis.



Further reading

- Royal College of Ophthalmologists: Referral Guidelines for adult ocular tumours
- The Liverpool Ocular Oncology Centre: A Guide For Practitioners

Uveal Melanoma

Beyond the Eye

Risk prediction of tumour spread is very important to uveal melanoma patients. The disease frequently spreads via the bloodstream, typically to the liver (90% of cases); close to 50% of uveal melanoma patients ultimately die of metastatic disease. There are clinical, histopathological, cytogenetic and molecular variables of the tumour cells that can be used to help predict this. Especially the presence of monosomy 3 (loss of one copy of chromosome 3) is a poor prognostic indicator. This testing can be performed on patients not only having surgical treatment of their melanoma, but also via an intraocular biopsy in those having radiotherapy. Discussions with the patients regarding genetic testing should take place prior to any therapy being undertaken.

Surveillance of the affected eye will depend on the type of treatment undertaken but is usually 6 monthly or annually. This may be shared between the supra-regional centre and the referring hospital.



Liver surveillance for distant metastases should take place in a centre with an MDT that incorporates expertise from ophthalmology, radiology, oncology, cancer nursing and hepatic services (liver surgery and interventional radiology). All uveal melanoma patients should receive at least annual imaging of the liver. Patients with a high risk of tumour spread should receive 6 monthly liver imaging. There is no consensus about what form this should take; however, evidence suggests that MRI can detect liver lesions earlier. This may allow for the liver tumour(s) to be removed surgically, resulting in prolonged survival. Centres may only provide ultrasound as an alternative.

Treatment for metastases

Uveal melanoma metastases can appear anywhere in the body, but typically they arise first in the liver, where they are often numerous and can grow very quickly, with a doubling time of as little as four weeks. Other common sites of metastases include the lungs and bone. The rarity of uveal melanoma and lack of close surveillance for secondaries have limited the evidence for treatments for metastases. There is currently no effective systemic, cytotoxic chemotherapy for metastatic uveal melanoma.

Resection of uveal melanoma liver metastases is proven to prolong survival when technically possible. In recent years there have been developments in the use of liver-directed therapies, such as liver surgery, TACE (transcatheter arterial chemoembolisation), SIRT (selective internal radioembolisation) and PHP (percutaneous hepatic perfusion). At present the evidence to suggest that non-surgical liver directed treatments extend a patient's overall survival is limited; however it seems sensible to use liver-directed therapy when the liver is the only site of disease and resection is not possible.

Immunotherapy is also an option, although it must be given early enough to allow time for it to work (12 weeks to 1 year). Ipilimumab (anti CTLA-4) is currently recommended by NICE for metastatic melanoma. At the time of writing, anti PD-1 drugs are in trial.

The genetic mutations thought to initiate uveal melanoma – GNAQ and GNA11 – are not currently therapeutically targetable. However, it is possible that biological therapies that target the same pathway, such as MEK inhibitors, could be useful in uveal melanoma. These are under trial.

Further reading

➤ The English Uveal Melanoma Guidelines can be found on the Melanoma Focus website – www.melanomafocus.org



About us

OcuMel UK aims to provide information and support to anyone affected by ocular melanoma who would be otherwise isolated. We also provide information to GPs.

We can be contacted via our helpline on **0300 790 0512** or email info@ocumeluk.org.

