



Uveal Melanoma: pathological aspects

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Declaration of Interests

- World Health Organisation
- Previously at U.K. NHS in Coventry. Previously a member of the ThermoFisher OncoNetwork Collaboration
- All opinions expressed are personal, and not those of any of the organisations above.

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Digestive System Tumours

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Tumours of the oesophagus

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2.0: Tumours of the oesophagus: Introduction

Lam
Ochiai
Odze R

AK
AO

This chapter describes benign and malignant tumours of epithelial differentiation and The ICD-O-4 topographical coding for ill ered in this chapter is presented in Box ; common benign lesion, squamous pap precursor lesions are typically describ from malignant tumours – a change line decision to make this change was bas expansion of our understanding of the b cal features of precursor lesions and th practice. There are two main types of precursor i que: Barrett dysplasia and squamous d 10 years or so, we have seen an impo towards ablation for the treatment of patients with high-grade dysplasia. The ally occur in the treatment of low-gr

Box 2.111 ICD-O-4 topographical coding for the anatomical sites covered in this chapter

2.1.2.2: Oesophageal squamous dysplasia

Takubo KT
Fuji SF

Definition
Squamous dysplasia of the oesophagus is an unequivocal neoplastic alteration of the oesophageal squamous epithelium, without invasion.

ICD-O coding
8077/00 Low-grade squamous dysplasia
8077/02 High-grade squamous dysplasia

ICD-11 coding
2E92.0 & XH3Y37 Benign neoplasm of oesophagus & Oesophageal squamous intraepithelial neoplasia (dysplasia), low-grade
2E90.1 & XH4ND8 Carcinoma in situ of oesophagus & Oesophageal squamous intraepithelial neoplasia (dysplasia), high-grade

Related terminology
None

Subtype(s)
None
Localization
Squamous dysplasia can occur anywhere in the oesophagus, and it is likely to follow the distribution of squamous cell carcinoma.

Clinical features
Patients at high risk of oesophageal squamous cell carcinoma are usually followed using a combination of Lugol's chromendoscopy and narrow-band imaging [1366]. With Lugol's iodine, low-grade dysplasia appears as an unstained or weakly stained area; high-grade dysplasia is consistently unstained [2974]. Features associated with neoplastic disease include large size, non-flat appearance, positive pink-colour sign, and multiplicity of distinct iodine-unstained lesions [3702]. On narrow-band

imaging, dysplastic lesions appear as areas of brownish discolouration [2250,2202]. Abnormalities on narrow-band imaging reflect the invasion depth of intramucosal carcinoma and changes of intrapapillary capillary loops [2458].



Fig. 2.111 Oesophageal adenocarcinoma. A Tubular pattern. B Papillary pattern. C Mucinous pattern. D Signet-ring cell pattern.

The mucosa adjacent to the adenocarcinoma may show Barrett dysplasia and intestinal metaplasia (Barrett oesophagus). Oesophageal adenocarcinomas can be classified as having tubular, papillary, mucinous, and signet-ring cell patterns. Only limited evidence of the relevance of these patterns is available; therefore, patterns are described rather than subtypes. A mixture of these patterns is often seen. The tubular pattern is most common. It is characterized by irregular, single or anastomosing tubular glandular structures lined by a layer of single or stratified malignant epithelium; neoplastic glands often show variable amounts of intracellular mucin production and may show dilatation [1756]. The papillary pattern is characterized by papillae, with rare cases showing micropapillary architecture [1182]. The mucinous pattern generally shows carcinoma cells floating in



Fig. 2.112 Oesophageal squamous dysplasia. A On low-magnification endoscopy with narrow-band imaging, B On high-magnification endoscopy with narrow-band imaging, C On white-light endoscopy. The lesion appears as a flat, pinkish lesion positive for the pink-colour sign – it is well demarcated and unstained.

Macroscopic appearance
Oesophageal adenocarcinomas often present in advanced stages and appear as stricture, polypoid, fungating, ulcerative, or diffuse infiltrating lesions. In earlier stages, adenocarcinomas may appear as irregular plaques. Early-stage carcinomas may present as small nodules or may not be detected on endoscopy. Adjacent to the carcinoma, there may be irregular tongues of reddish mucosa (resembling a salmon patch) that represent Barrett oesophagus and reflux changes and that contrast with the greyish-white colour of the squamous-lined oesophageal mucosa.

Histopathology
Oesophageal adenocarcinoma shows gastric, intestinal, and mixed (hybrid) lineages, evidenced by a combination of morphological and immunohistochemical features [1548,426].




Fig. 2.113 Oesophageal adenocarcinoma. An example in Barrett oesophagus with a double layer of muscularis mucosae.

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BOOKS CATALOG

Digestive System
ONLINE




Digestive system tumours (5th ed)

Breast
ONLINE




Breast tumours (5th ed, beta version)

Endocrine System
ONLINE




Endocrine tumours (4th ed)

Eye
ONLINE




Eye tumours (4th ed)

Skin
ONLINE



Skin tumours (4th ed)

Head and Neck
ONLINE

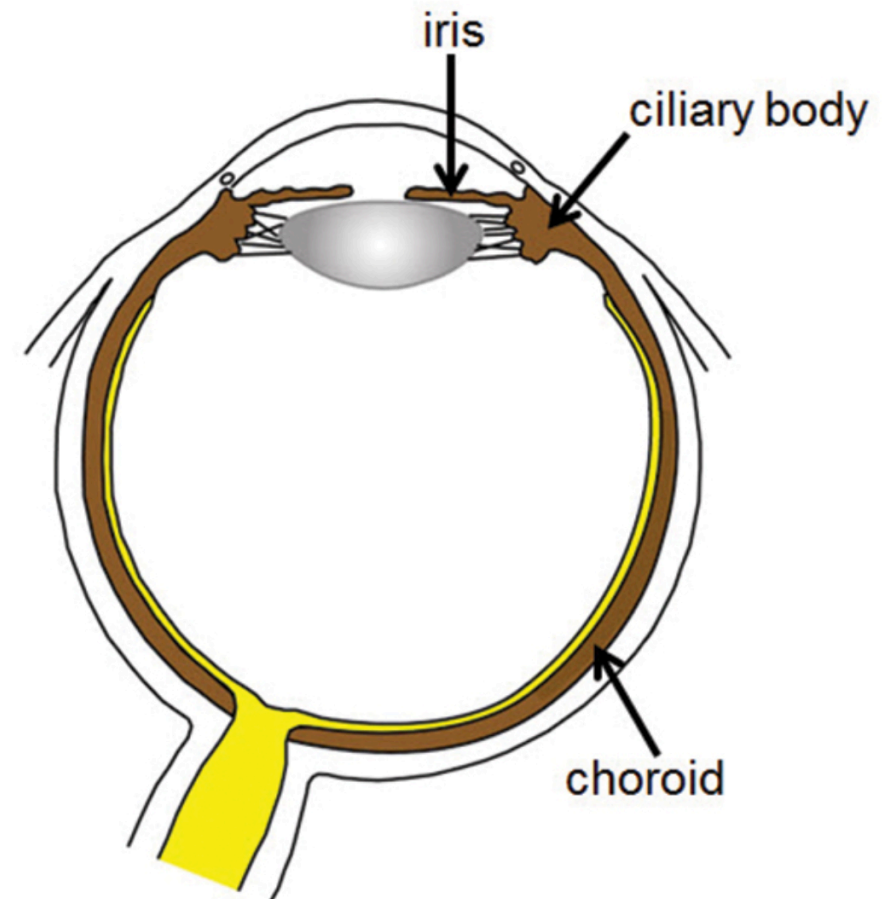
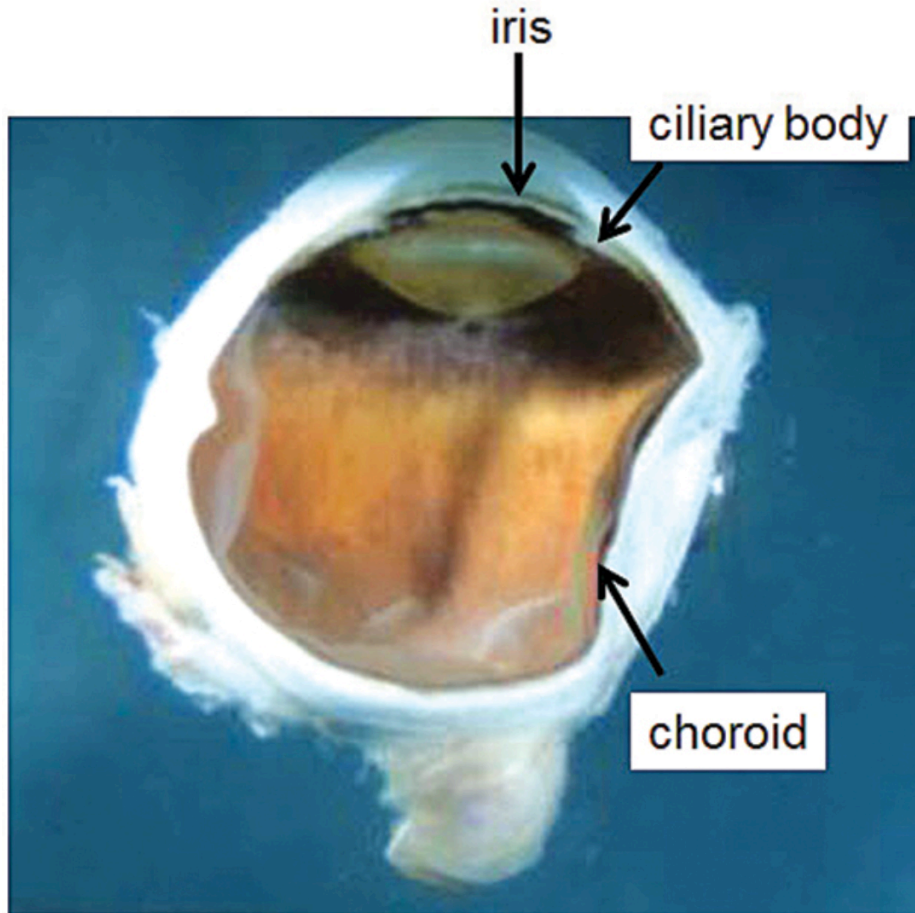



Head and neck tumours (4th ed)

Uveal Melanoma

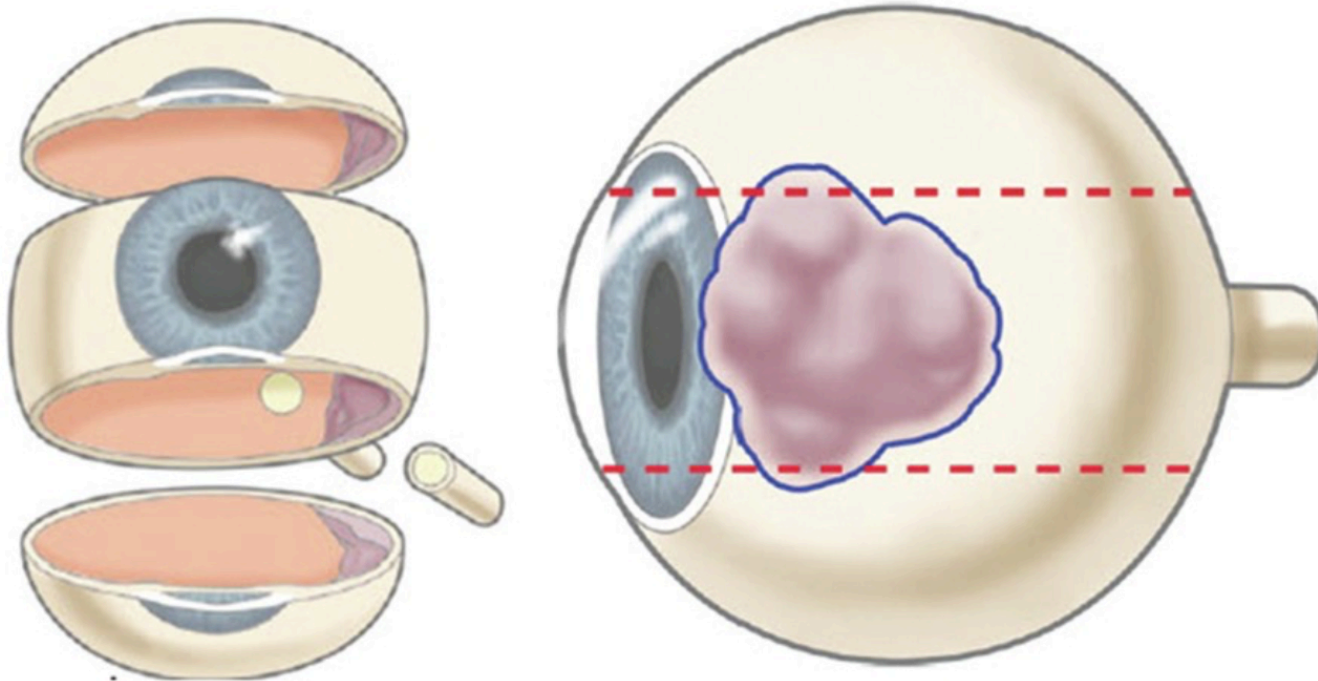
- Definition: Primary malignant melanocytic tumours of the uveal tract: Choroid, Ciliary Body (CB) and Iris.
- Diagnosis: Usually clinical by ophthalmoscopy during routine eye exam – only 25% have symptoms.
- Circumscribed and nodular – may hide behind iris.
- CB melanoma may cause glaucoma by anterior displacement of the lens-iris diaphragm, tumour seeding, iris neovascularization, or rarely by pigment dispersion.
- Choroidal lesions domes-shaped (75%), mushroom shaped (with retinal detachment, of diffuse (5%).
- Pigmented in 55%, but non-pigmented in 15%.

Anatomy



 uveal tract

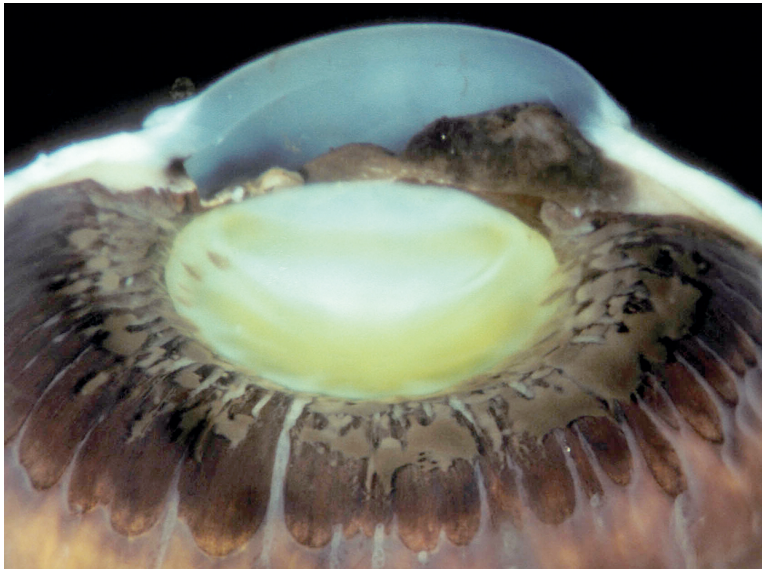
Macroscopic dissection



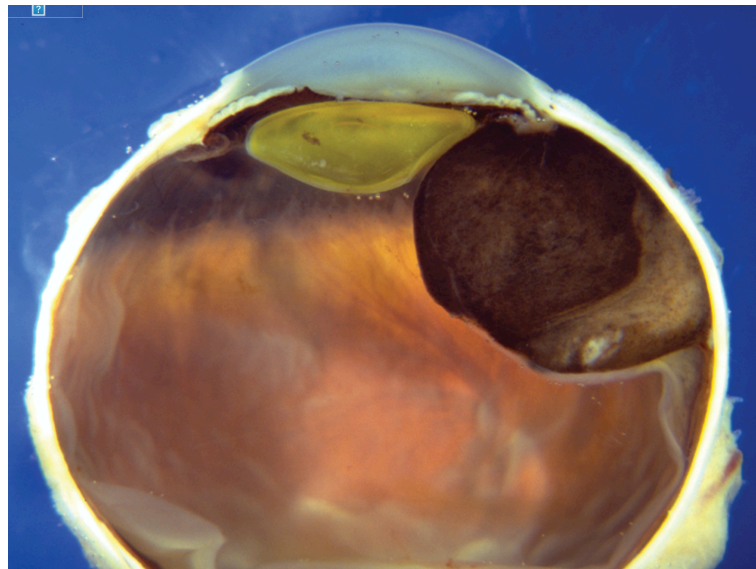
- Observe
- Transilluminate
- Cut culottes either side of tumour
- Embed on best side, and culottes
- Cut levels!

Macroscopic appearance

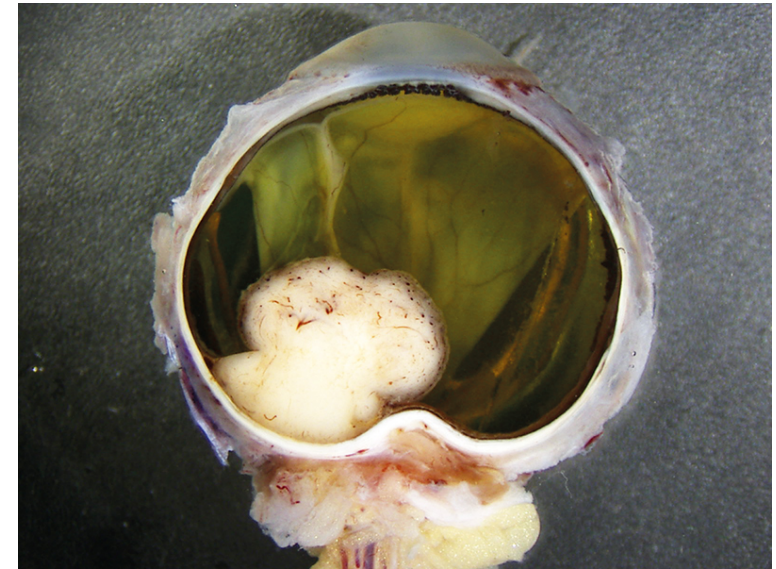
Iris Melanoma



CB Melanoma



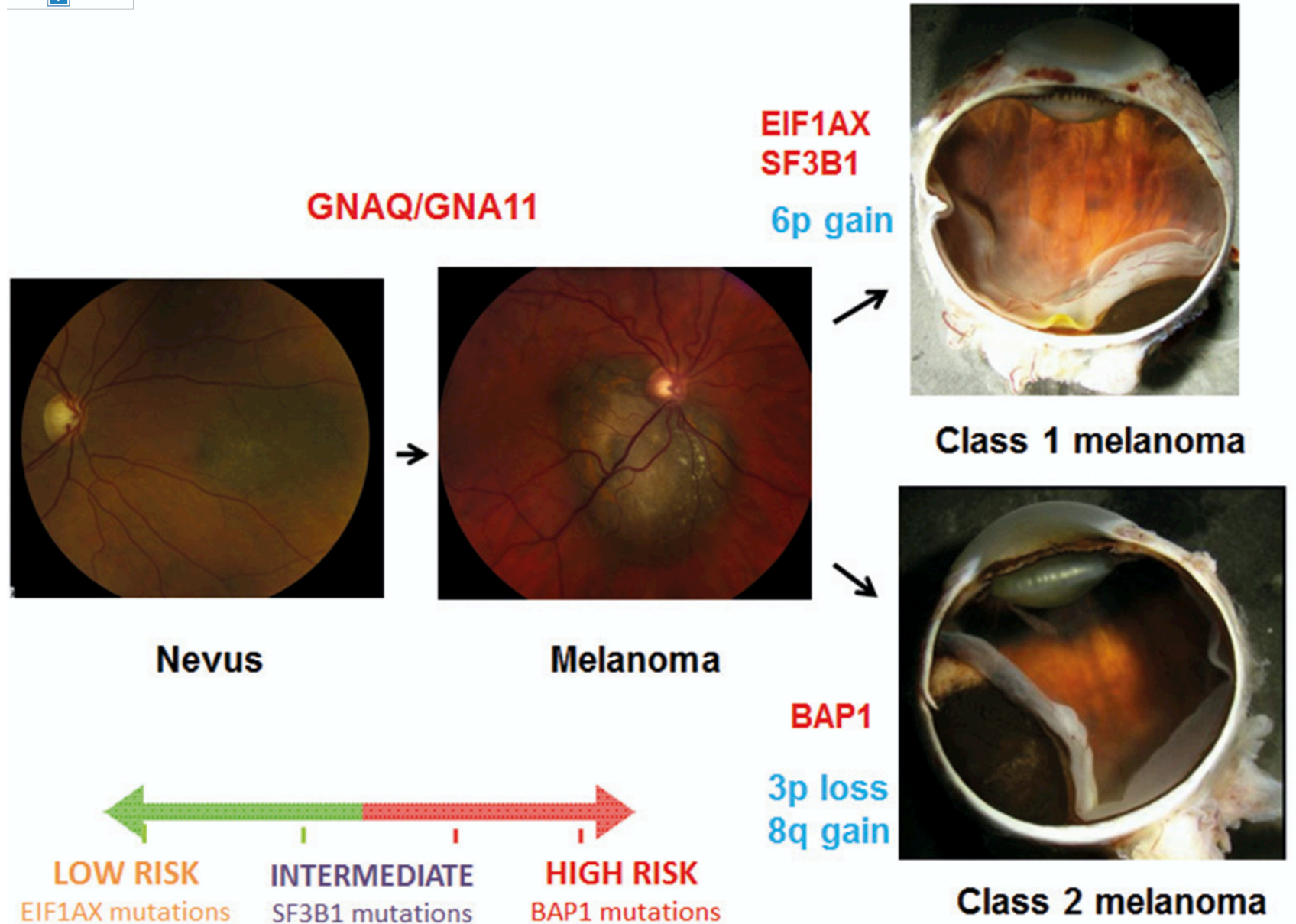
Choroidal Melanoma



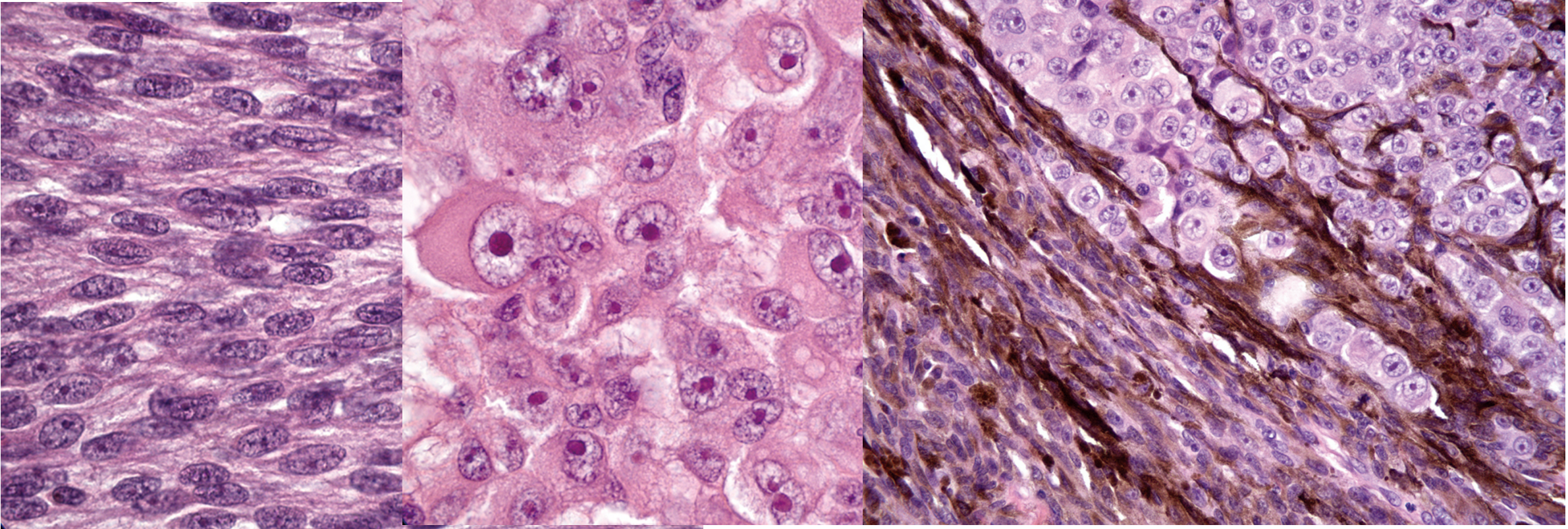
Epidemiology

- Worldwide, the incidence rate is about 2–8 cases per 1 million person-years – lower at lower latitudes (1.3–2.9 cases per 1 million person-years) and increasing with latitude (to 6.1–8.6 cases per 1 million person-years)
- Risk factors include uveal naevus (1 in 400), light skin pigmentation, blonde or red hair, dysplastic naevus syndrome, or BAP1 tumour syndrome.
- UV has no definite role. There is an association with welding.

Genomics of Uveal Melanoma



Histopathology – Choroid

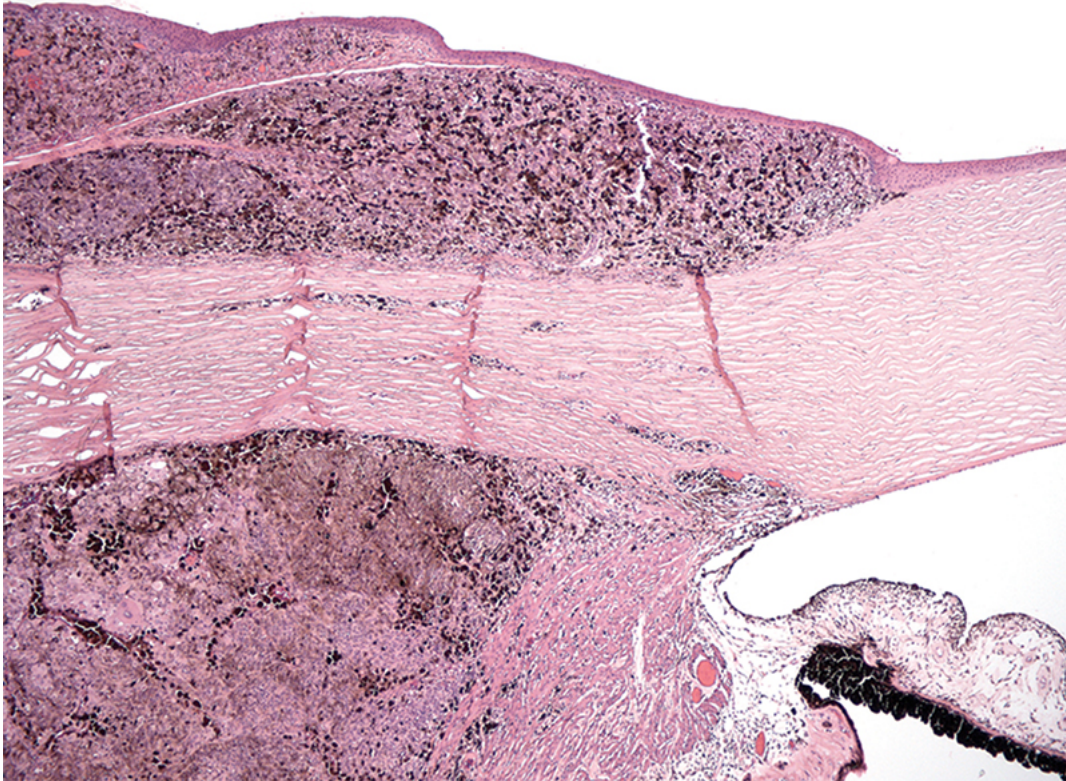


Spindle B cells

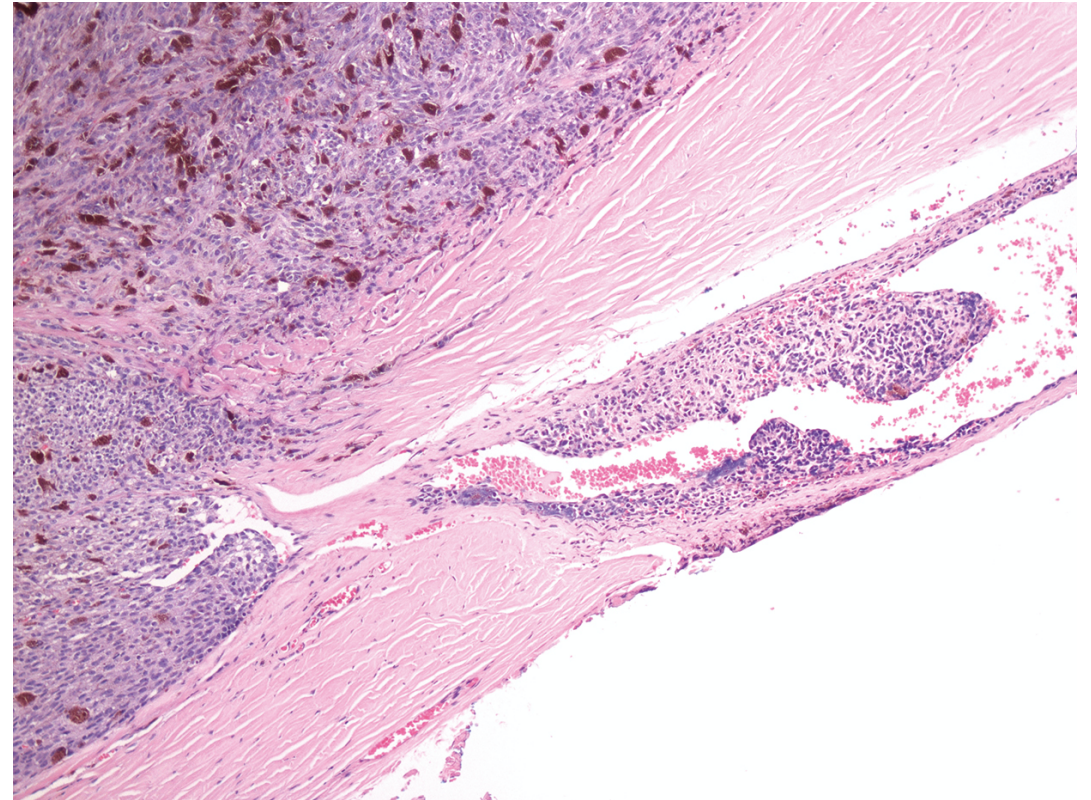
Epithelioid cells

Mixed cells

Histopathology – Local spread

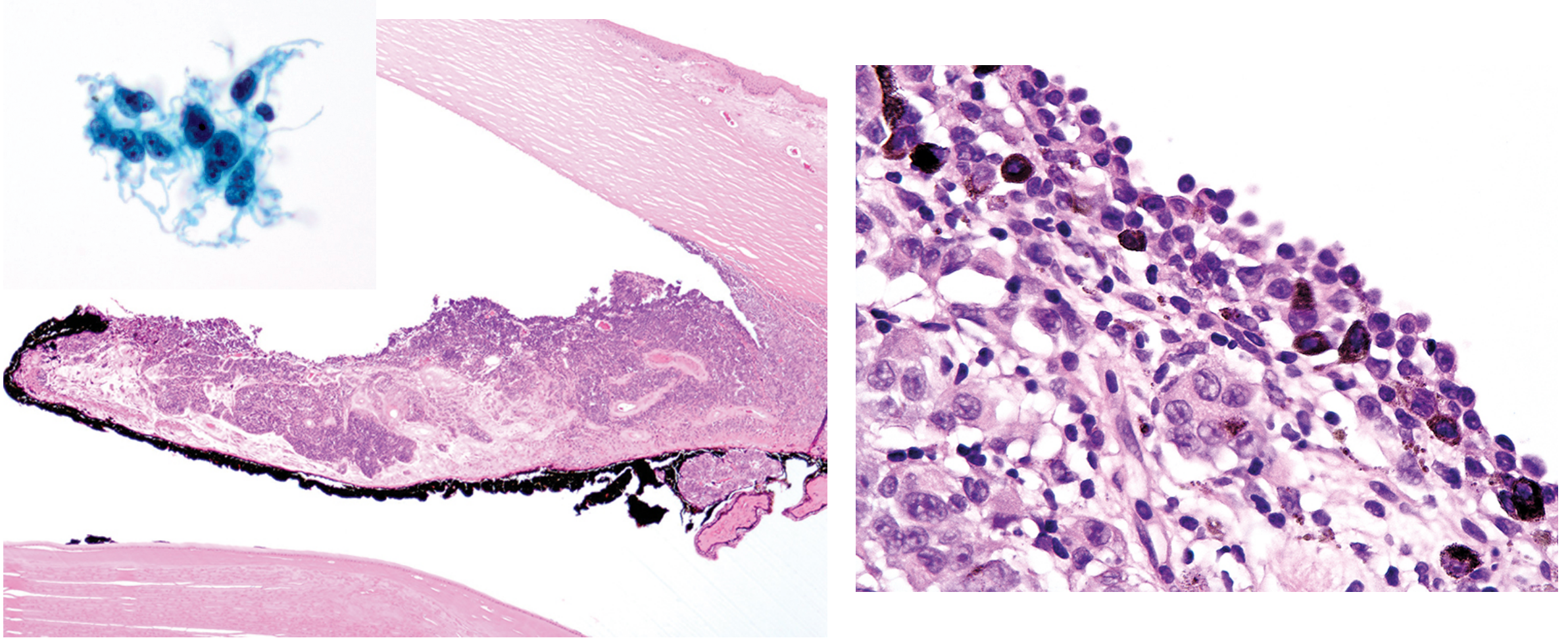


Collecting duct involvement

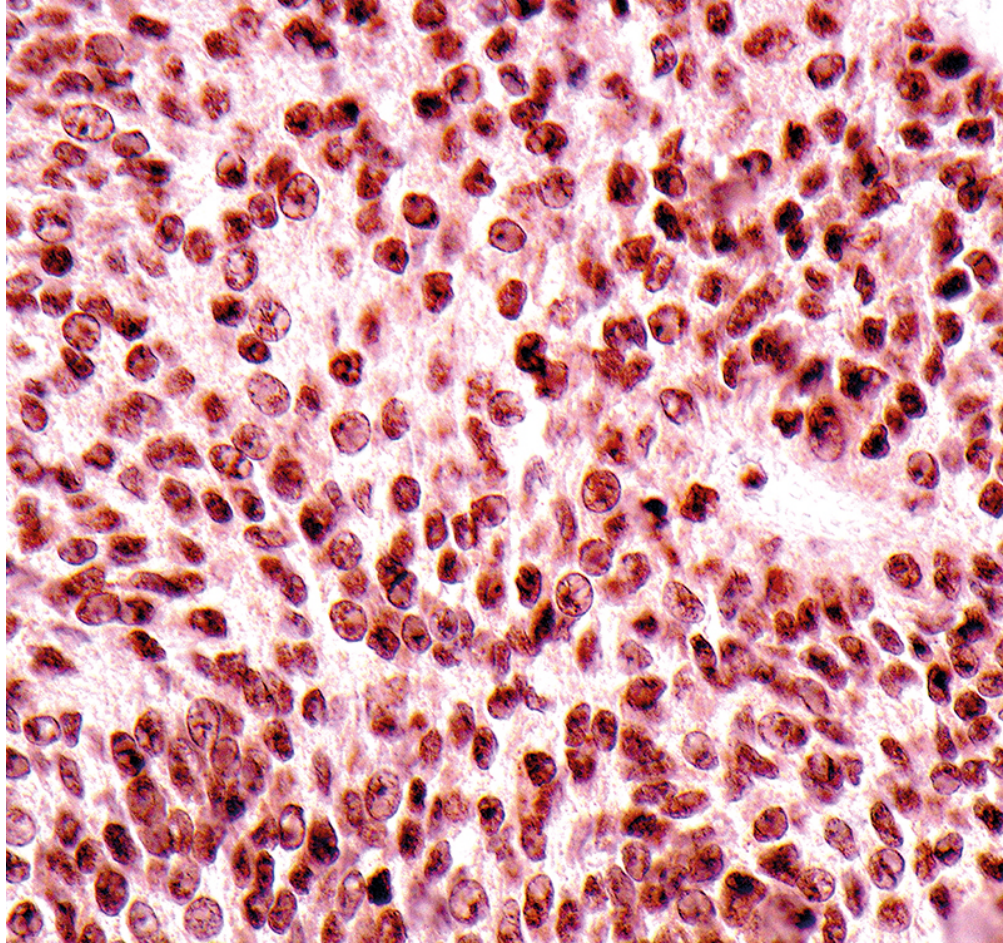


Vortex vein involvement

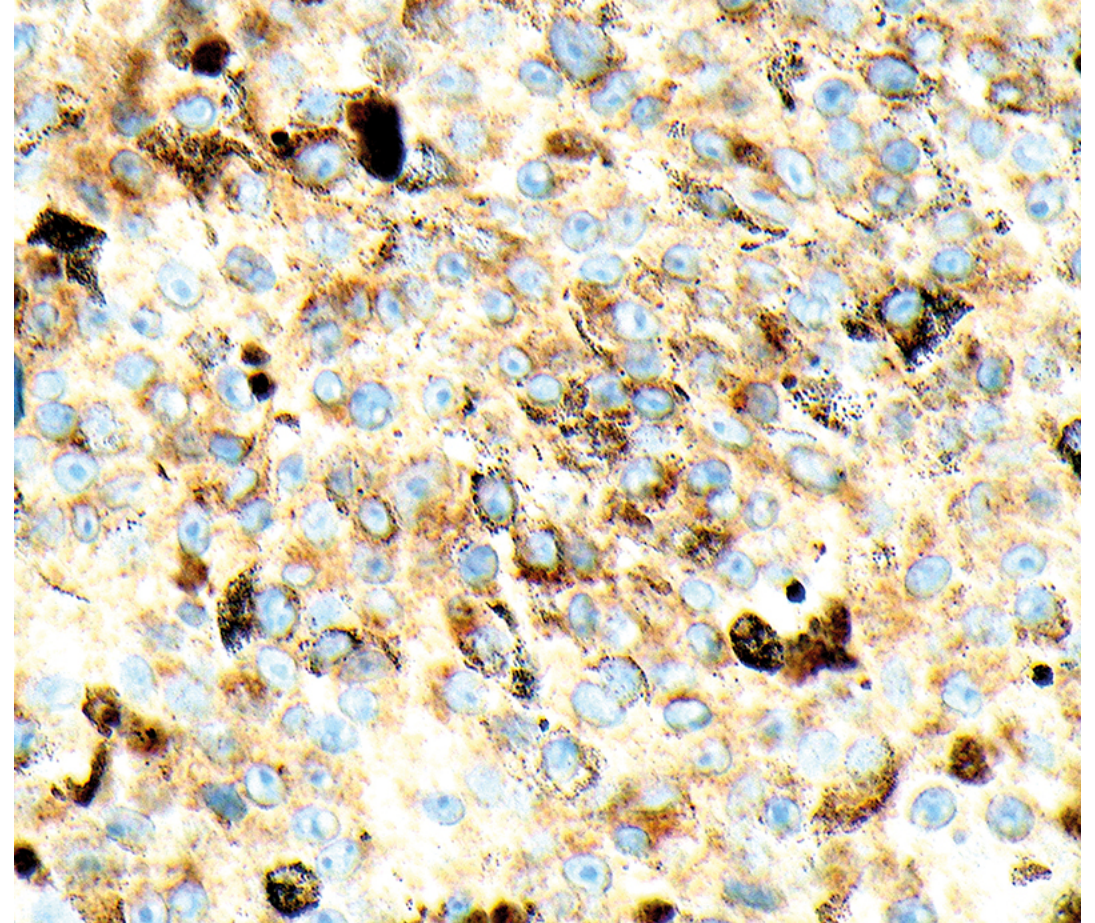
Histopathology – Iris melanoma



BAP1 immunohistochemistry

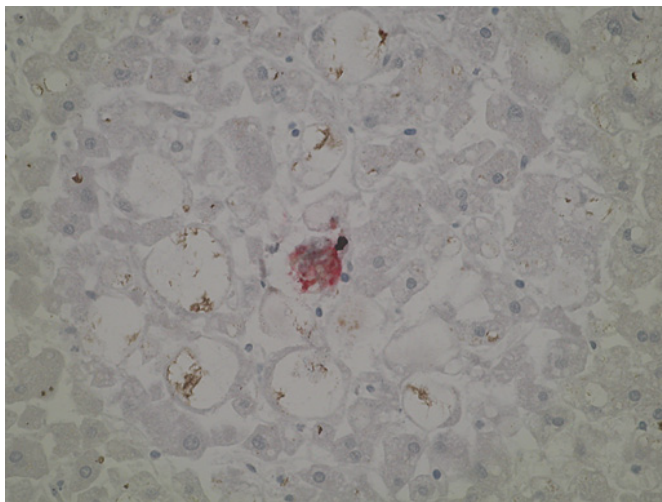
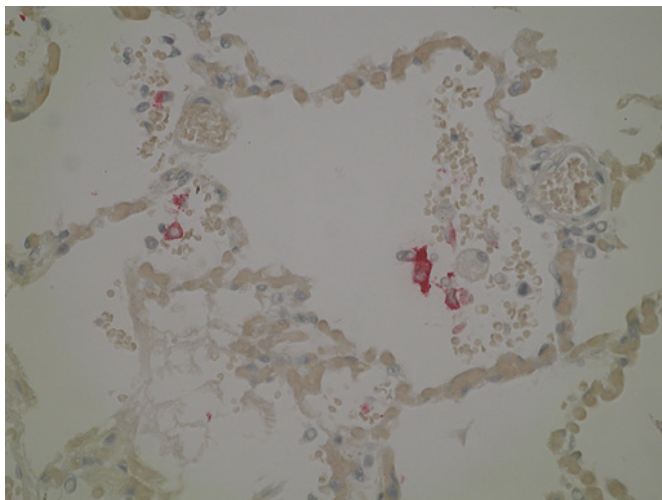


BAP1 is positive in the nuclei.



BAP1-negative choroidal melanoma.

Micrometastasis



Tumour latency:

- Immune control of metastatic cells
- Lack of angiogenesis
- Reduced cell turnover/growth.

No evidence of multicellular micrometastases, so option 3 most likely.

Conclusions

- Uveal melanomas may arise from the iris, ciliary body, or choroid.
- Anterior tumours may invade the collecting ducts and gain access to conjunctival lymphatics
- Posterior tumours may invade vortex veins leading to haematogenous spread, often to lungs or liver
- 50% of patients die from haematogenous spread: as well as size, cell type, and vascularity, identification of tumours with BAP1 loss has prognostic significance.

Thank you!



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