

Letter to the Editor

Two different tumours in the same eye

Benign and malignant intraocular pigmented lesions can share similar clinical and diagnostic signs, posing a challenge for the clinician ophthalmologist.¹ We report a case of a retinal pigment epithelium (RPE) adenoma imitating a malignant transformed melanocytoma at the optic nerve, 10 years after treatment of a peripheral choroidal melanoma in the same eye. According to our knowledge, this is the first report of a choroidal melanoma and an RPE adenoma in the same eye.

A 54-year-old woman was diagnosed with a peripheral choroidal melanoma in the right eye and underwent ruthenium plaque radiotherapy. At that time, a presumed melanocytoma of the optic disc was documented in the same eye. The left eye was unremarkable. Ten years after melanoma treatment, the patient complained about metamorphopsia and progressive visual loss. On examination, best-corrected visual acuity was 6/38 oculus dexter (OD) and 6/6 oculus sinister (OS). The intraocular pressure was 18 mmHg OD and 20 mmHg OS. There was no significant change to the pigmented lesion at the right **Q2** optic disc compared with previous findings (Fig. 1a). **Q3** On ultrasonography, the tumour measured 3.54 × 3.71 mm with a thickness of 1.73 mm. The previously treated choroidal melanoma in the superior periphery had regressed completely. Six months later, however, the pigmented tumour at the optic

nerve showed a slight increase in growth, measuring 4.09 × 3.97 mm with a thickness of 1.64 mm. A vitrectomy with silicone oil tamponade and a transretinal biopsy of the presumed melanocytoma with the 25-gauge vitreous cutter were conducted 8 months later because of an exudative retinal detachment. The cytological examination suggested a pigmented tumour, predominantly of small plump cells with oval-shaped nucleus and with a discrete central nucleolus. The molecular diagnostics using microsatellite analysis revealed an allelic imbalance and loss of heterozygosity for one of the four examined loci on chromosome 3p as well as for one locus on chromosome 3q, suggestive (but not conclusively) of the diagnosis of a spindle cell choroidal melanoma.

A further 2 months later, the patient re-presented with a rhegmatogenous retinal re-detachment in the right eye. Best-corrected visual acuity was hand motion OD and 6/6 OS. Both eyes were normotensive. On the grounds of significantly reduced vision and the suggested diagnosis of a malignant transformation of the presumed melanocytoma into a melanoma, enucleation of the right eye was decided on by the patient.

The enucleation specimen revealed chorioretinal atrophy at the level of the equator, corresponding to the area of the previously treated choroidal melanoma. At the optic disc, a nodular proliferation of RPE cells in the form of pseudoglands and trabeculae was seen (Fig. 1b). Some of the RPE cells were pigmented. **Q4** The cells were small-to-medium in size with ovoid nuclei and prominent nucleoli. Mitoses were not seen. The lesion was contiguous with the

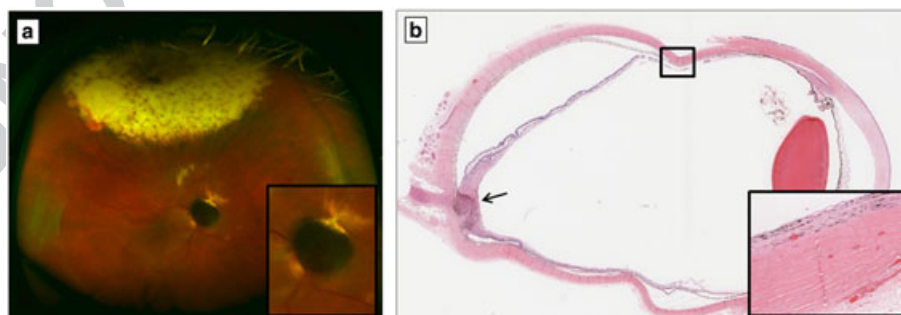


Figure 1. Ophthalmoscopic image and histology of the right eye. (a) Ophthalmoscopic image demonstrating the black pigmented tumour at the optic disc and the area of plaque irradiation superiorly. Inset, magnified view of the lesion of concern at the optic disc. (b) Enucleation specimen showing a chorioretinal atrophy following plaque brachytherapy and a nodular proliferation of the retinal pigment epithelium (RPE) (arrow) at the optic disc (hematoxylin–eosin, original magnification × 1.5). Inset, magnified view of the area in the choroidal and retinal atrophy (hematoxylin–eosin, original magnification × 10).

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adjacent RPE layer. On immunohistochemistry, these cells were strongly positive for MelanA, Ki-67 and the cytokeratin stain AE1/AE3 as well as for F2 CAM5.2 (weak; Fig. 2b,c,d). Nuclear staining for microphthalmia transcription factor was seen. They were negative for the cytokeratin markers CK5/6, CK7 and MNF-116, as well as for the melanocyte markers SOX10 and HMB-45. These histological findings led to the diagnosis of an RPE adenoma at the optic nerve.

We report a rare case of two different tumour entities in the same eye. The coexistence of two or more neoplasms in the same eye is very uncommon and can be diagnostically challenging.^{2,3} To date, the occurrence of an RPE adenoma and a choroidal melanoma has not been described in the literature.

There are some similarities among RPE adenomas, choroidal melanocytomas and melanomas; however, there are usually distinct clinical signs for differentiating these neoplasms.⁴ Despite this, in some cases, the differentiation between these entities can be difficult and requires pathological analysis.

In the present case, it was clear that the peripheral choroidal tumour was a melanoma and was treated as such. The initial clinical diagnosis of an additional optic disc melanocytoma – a benign lesion, which may enlarge on follow-up examination but otherwise seldom causes further ocular complications⁵ – was based on the tumour's location, size, shape, degree

of pigmentation and on fluorescein angiography characteristics. The latter tends to demonstrate hypofluorescence in these lesions. A late pooling of dye can be seen if secondary optic disc oedema and/or subretinal fluid are present.⁵ Ultrasonography is of low diagnostic value because of the small size of melanocytomas and the mean thickness of less than 1 mm.⁵ Only 1–2% of ocular melanocytomas will undergo transformation into melanoma.

Similar to choroidal melanocytomas, RPE neoplasms can present as dark brown or black lesions.⁴ RPE tumours appear as abruptly elevated masses arising perpendicularly and usually lack the adjacent base that is seen with most choroidal melanomas or melanocytomas.⁴ It is reported that RPE adenomas rest upon Bruch's membrane and do not produce the characteristic mushroom configuration of some melanomas.⁴ However, RPE adenomas can induce yellow retinal or subretinal exudation and ultimately exudative retinal detachments.⁴ Tumours of the RPE show prominent feeder vessels in arterial phase and tend to be hypofluorescent in the filling stages. This is in contrast to choroidal melanomas, which show a dilated tortuous vein and an early hyperfluorescence and intense late staining.⁴ On ultrasound, RPE adenomas show high internal reflectivity with A-scan and a dome-shaped mass with acoustic hollowness with B-scan compared with the low internal reflectivity of the choroidal melanoma.⁴

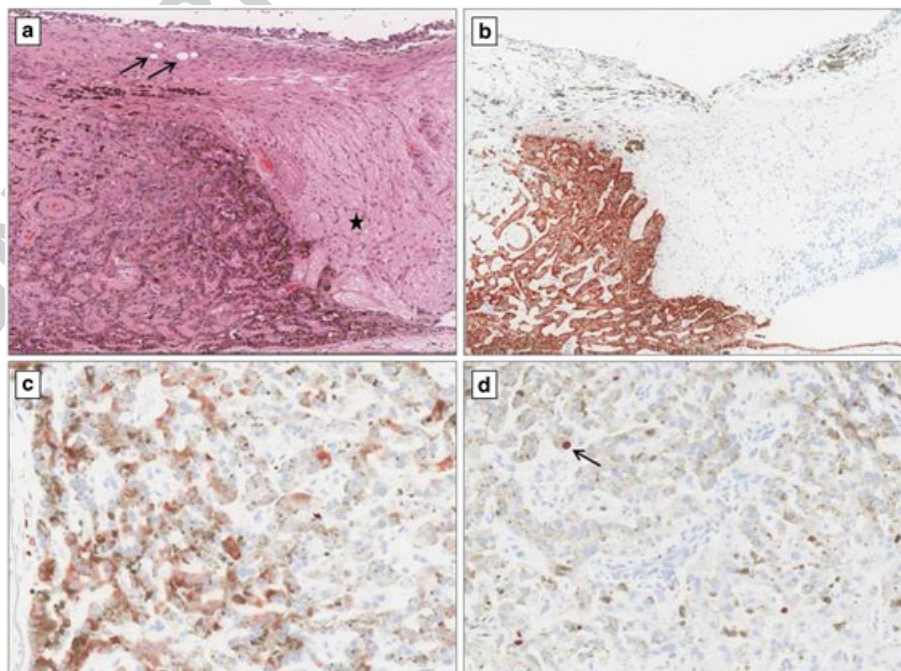



Figure 2. Immunohistochemical staining of the enucleated specimen. (a) Hematoxylin–eosin staining demonstrates the adenoma of the RPE, with the adjacent disorganised retina showing gliosis (asterisk) and occasional silicone oil droplets (arrows) (original magnification $\times 20$). (b) Immunostaining using AE1/AE3 indicates that the pigmented tumour has arisen from the RPE, which at the right has a regular structure (original magnification $\times 20$). (c) The RPE adenoma demonstrated patchy immunoreactivity for MelanA (original magnification $\times 40$). (d) A very low Ki-67 growth fraction (arrow) (original magnification $\times 40$).

Cytological analysis demonstrates deeply pigmented, plump, round cells with large melanosomes and rare mitotic figures in RPE adenoma cases compared with the spindle cells that characterize most melanomas.^{4,6} Because of its rarity, the immunohistochemical characteristics of the RPE adenoma have not been extensively described. In contrast to melanoma, RPE adenoma is negative for HMB-45 and cytokeratin 7.⁶ Instead, RPE may be positive for epithelial membrane antigen, S-100P, neurone-specific enolase, synaptophysin and vimentin.⁶ To date, the genetic changes of RPE adenomas are not known.

This case demonstrates the clinical complexity of differentiating pigmented intraocular lesions as well as the rarity of two different neoplastic entities in the same eye. Further investigation of the molecular and immunohistochemical features of RPE adenoma would aid the diagnostic process in unclear cases and enhance the therapeutic approach for the affected patients.

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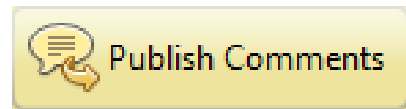
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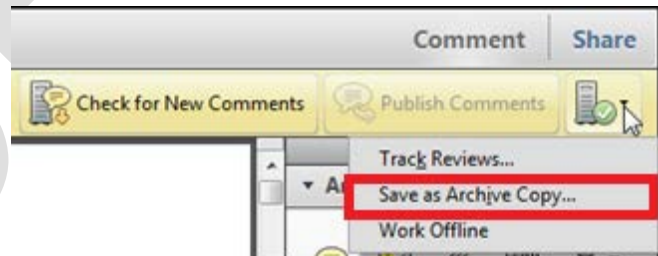
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