Adenocarcinoma of retinal pigment epithelium

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SUMMARY This report describes a 41-year-old man with an intraocular tumour misinterpreted clinically as choroidal melanoma. The fluorescein angiographic features were not fully characteristic of uveal malignancy, and indeed histopathology revealed the diagnosis of adenocarcinoma of the retinal pigment epithelium. It is suggested that, in cases with the fundus and angiographic findings described here, the rare possibility of adenocarcinoma of retinal pigment epithelium should be kept in mind. Of particular interest were the changing pathological findings in the various parts of the tumour, which paralleled the fluorescein angiographic pattern.

Adenocarcinoma of the retinal pigment epithelium is a very rare neoplasm which is notoriously difficult to diagnose clinically and has always prompted enucleation because of its resemblance to choroidal melanoma.¹⁻⁵

This report describes the case of a male patient who underwent enucleation for a retinal mass that looked like a melanoma and seemed to grow during a follow-up period of one year. The angiographic characteristics were not fully suggestive of melanoma, and indeed the histopathological studies revealed the tumour to be an adenocarcinoma of the retinal pigment epithelium. In such a rare condition, where reports on individual patients constitute the main source of knowledge of the tumour characteristics, it seems worthwhile to publish our case, both for what it illustrates and for the areas of ignorance it exposes.

Case report

A 41-year-old male was admitted for investigation following the diagnosis of an intraocular tumour in his left eye. The initial symptoms had appeared six months before admission, when he complained of metamorphopsia and disturbances of visual acuity in his left eye.

Ocular examination revealed an entirely normal right eye with 20/20 visual acuity. In his left eye the vision was 20/40, the intraocular pressure was normal, and no anterior segment abnormalities were present,

except for a few cells in the anterior part of the vitreous.

Ophthalmoscopic examination disclosed in the upper temporal quadrant of the left fundus a well defined pigmented mass, abruptly protruding into the vitreous (Fig. 1). The lesion occupied an area of about 5 disc diameters and was more pigmented in its nasal side. Some subretinal glial reaction was seen in its inferonasal border, which was continued by a serous detachment extending towards the macula. The retinal vessels adjacent to the tumour were dilated and tortuous along the whole of their length. No orange discolorations or drusen were disclosed on the surface of the tumour.

On fluorescein angiography the tumour failed to show uniform fluorescence (Fig. 2). In its nasal part no fluorescence was disclosed throughout the entire angiographic study. The temporal part of the tumour on the other hand showed early hyperfluorescence, which gradually increased in intensity. The two afferent arteries – one dilated and the other of normal calibre – filled rapidly and seemed to penetrate the tumorous mass (Fig. 2). The tortuous efferent vein was rapidly filled by fluorescein, indicating increased volume of flow through a possible arteriovenous shunt. The sensory retinal elevation appeared in the lower part of the tumour (Fig. 3). The retinal gliosis adjacent to the nasal border of the tumour showed late staining (Fig. 4).

Laboratory and general medical evaluation failed to provide any pertinent findings that could have been related to the ocular lesion.

During the following year the tumour increased slightly in size. As the general consensus of opinion

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Fig. 1 The tumour located temporally to the macular region, jet black in its nasal part and discoloured on the temporal side (red-free).

was that the lesion could be a choroidal melanoma, surgery was recommended. The patient underwent an uncomplicated enucleation, and no extraocular extension was noted at the time of operation.

PATHOLOGICAL FINDINGS

The specimen consisted of an intact left eye. The globe transmitted light readily except for a round area of about 6 mm in diameter on the temporal side. The globe was sectioned, and a well demarcated, heavily pigmented tumour appeared in the supero-temporal quadrant.

A marked variation in the histological structure of the nasal and temporal side of the tumour was observed (Fig. 5). In the nasal part the pigmentary content of the tumour as a whole was higher, the cells were more densely arranged, and they were separated by less stromal tissue. On the temporal side the tumour contained areas of low cell density with more abundant stroma. The penetrating afferent artery could also be visualised in the histological preparation (Fig. 5).

The tumour mass was composed of cuboid or columnar pigmented epithelial cells typically

Fig. 2 On the arterial phase of the angiogram the tumour remains hypofluorescent in the nasal part, and one of the afferent arteries which seems to penetrate the mass is dilated. The efferent vein is tortuous and fills precociously.

Fig. 3 Arteriovenous phase of the angiogram with sensory retinal elevation on its inferior part.

Fig. 4 Late non-homogeneous staining of the tumour.

arranged in pseudoglandular pattern (Fig. 6). They were attached to membrane-like structures. In routine haematoxylin-eosin preparations the cells were so deeply pigmented that cytological details were not discernible. In bleached histological sections the tumour cells appeared as clusters of epithelial cells varying in shape and having an adenoid disposition (Fig. 7). Mitotic figures were rarely seen, and the occasional cells in mitosis had sparsely pigmented granules. The cytonuclear anomalies were characterised mainly by giant nuclei with prominent nucleoli (Fig. 8).

Along the surface of the choroid, round the border of the tumour, recognisable retinal pigment

epithelium appeared to change its structure from normal to abnormal morphology. The Bruch's membrane was intact on all the sections examined (Fig. 5). At the nasal border of the mass the adjacent retina underwent gliosis. In some parts of the preparation tumour cells directly invaded the retinal layers, which were totally destroyed over the dome of the lesion.

Discussion

Adenocarcinoma of the retinal pigment epithelium is an infrequently encountered tumour which may masquerade as choroidal melanoma. Its rarity and the usual failure to diagnose it clinically has precluded successful recognition before enucleation and histopathological examination. A review of the literature confirms that clinical and angiographic descriptions of histologically proved adenocarcinoma of the retinal pigment epithelium have been few, and its appearance in a male subject seems to be exceedingly rare.^{1,3,4}

The histological examination in our case was crucial, and its results were characteristic enough to make the correct diagnosis. The tissues in the vicinity of the tumour and its continuation with normal retinal pigment epithelium led us to believe that the mass represented a neoplasm of pigment epithelial origin. The intact Bruch's membrane also supported the pigment epithelial origin of the tumour without the issue being clouded by simultaneous choroidal involvement. Its invasive nature to the adjacent layers and its pseudoglandular configuration pointed to the diagnosis of adenocarcinoma. The tumour did not appear to be malignant cytologically, nor did it develop any metastases during a seven year follow-up.

Fig. 5 General histological aspect of the tumour, retinal vessel penetrating the mass. Note the regional differences in pigmentation of the tumour tissue and the intact Bruch's membrane.

Fig. 6 Pseudoglandular disposition of the tumour cells.

The opportunity of demonstrating the angiographic pattern of this case and its correlation with the tumour's structural characteristics were unique. Fluorescein angiography revealed some of the gross anatomical features of the tumour, and it was of assistance in detecting and defining some of the structural alterations in the tumour tissue. The nasal side of the mass showed no evidence of fluorescence either early or late in the study, and the tumour in this region appeared darker than on its temporal side. The presence and significance of these regional differences in fluorescein patterns was clarified by histological study, which correlated well with the angiographic results (Table 1). The inability to detect fluorescence on the nasal side of the tumour was thought to be due to the dense pigmentation acting as a barrier and so preventing the exciter light source from activating the fluorescein. However, on the temporal side, where the pigment was sparser and the amount of extracellular space larger, fluorescein

Table 1 Ophthalmoscopic and histological correlations

Biomicroscopy	Angiography	Histopathology
Nasal third of the tumour jet black	Early and late hypofluorescence (blocked hypofluorescence)	Very dense pigmented cells with pseudoglandular pattern in a reduced stromal area
Temporal part of the tumour showing discoloration	Early and late hyperfluorescence (window defect and late staining)	Sparsely pigmented cells in a more abundant stroma
Glial proliferation	Late staining	Retinal gliosis
Serous retinal detachment	Sensory retinal elevation	Cystoid retinal oedema
Afferent artery and efferent vein	Early and rapid filling, high volume of flow	Artery found in the tumour; presumed arteriovenous shunt

readily diffused into the more abundant tumour stroma.

Some additional aspects of the ophthalmoscopic features which may shed light on the clinical diagnosis of this condition merit specific attention. The intensely black colour of the tumour, its abruptly ascending borders, the dilatation of the adjacent retinal vessels, and the lack of surface orange discolorations could suggest that this case did not present a typical choroidal melanoma. Angiography indicated an increased intravascular volume, and the changes in the haemodynamics were thought to be produced via an arteriovenous shunt. Retrospectively it seems that awareness of all these characteristics and their correct interpretation could have obviated the mistaken diagnosis. Although the specificity of such features is not sufficiently high

Fig. 7 Bleached section with adenoid disposition of the tumour cells.

Fig. 8 Bleached preparation showing the giant nuclei with prominent nucleoli (arrow).

to allow complete dependence on them, it seems prudent to observe patients with enlarged afferent and efferent vessels leading to a pigmented retinal tumour over a longer time.

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