CASE REPORT

Adenocarcinoma of the pigmented ciliary epithelium

Aoi Sukeda,¹ Taisuke Mori,¹ Shigenobu Suzuki,² Atsushi Ochiai¹¹Department of Pathology and Clinical Laboratories, National Cancer Center Central Hospital, Tokyo, Japan²Department of Ophthalmic Tumor, National Cancer Center Central Hospital, Tokyo, Japan

Correspondence to

Dr Taisuke Mori,
tamori@ncc.go.jp

Accepted 28 June 2014

SUMMARY

Adenocarcinoma of the pigmented ciliary epithelium is an exceptionally rare eye tumour, with only a few cases reported to date. We encountered such a case in a 50-year-old woman who reported seeing floaters in her right eye. Fundus examination and MRI revealed an elevated lesion located in the ciliary body compressing the lens. The ciliary body was resected under the diagnosis of ciliary adenoma. On histological examination, the tumour exhibited epithelial features with glandular formation and moderate nuclear pleomorphism. The tumour invaded the subepithelial stroma of the ciliary body. Immunohistochemical findings were positive for cytokeratin OSCAR, AE1/AE3, CK7, EMA, S100, Melan A, HMB45, and microphthalmia-associated transcription factor.

BACKGROUND

Adenocarcinoma of the pigmented ciliary epithelium is an exceptionally rare tumour of the ciliary body, which may be classified as malignant, pigmented, acquired and neuroepithelial.¹

Tumours of the retinal pigment epithelium are classified as metastatic neoplasms or neuroepithelial tumours. Furthermore, Zimmerman² suggested that neuroepithelial tumours of the ciliary body can be divided into two groups, namely congenital and acquired tumours. Acquired neuroepithelial tumours, either benign or malignant, are observed mainly in adults and are composed of histological elements that resemble the fully differentiated ciliary epithelium. Benign neuroepithelial tumours, including pseudoadenomatous hyperplasia and adenoma, are rare. Additionally, malignant neuroepithelial tumours, including adenocarcinomas of pigmented and non-pigmented ciliary epithelia, are extremely rare, especially the pigmented ones.¹ Thus, more cases need to

be accumulated to clarify its behaviour. We report an extremely rare case of adenocarcinoma of the pigmented ciliary epithelium.

CASE PRESENTATION

Clinical history

A 50-year-old Japanese woman presented to our hospital because of a mass in her right eye. She had been seeing floaters in her right eye for 3 months before presentation. Fundus examination and MRI revealed that the mass presented with slightly low intensity on T2-weighted images, and it appeared to adhere to the ciliary body, compressing the lens (figure 1A). The typical choroidal melanoma is dome-shaped or mushroom-shaped with a basal dome-shaped portion, and it presents with very low intensity on T2-weighted images. The present patient had a round-shaped tumour without the basal component, which is not typical for melanoma. This tumour exhibited a slightly lower intensity than vitreous cavity and grey matter, but a higher intensity than white matter on T2-weighted images, which is also not typical for melanoma.

Case

Macroscopic findings

The mass arising from the ciliary processes was oval, and it measured 12×11×6 mm. The cut surface appeared black with yellowish-white focal colouration (figure 1B).

Microscopic findings

The tumour cells had abundant slightly eosinophilic cytoplasm. One-third of the tumour cells were abundant in brownish granules (figure 2A, B). Myxoid change was also observed. The mean mitotic activity was 2/10 high-power fields.

Figure 1 (A) MRI of the eyes. The mass showed low intensity on T2-weighted images, and it appeared to adhere to the ciliary body in the right eye (arrow heads). (B) Macroscopic features of the resected specimen. A gross photograph of the tumour focally showing a black and yellowish-white surface.

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To cite: Sukeda A, Mori T, Suzuki S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-204534

Figure 2 Microscopic features and immunohistochemical features. The tumour had pigmented and non-pigmented areas (A; low magnification). Both the pigmented area (B; high magnification) and the non-pigmented area (inset) showed the presence of epithelioid cells surrounding thin marked vessels. The invasive site of tumour cells and background ciliary epithelium stained with H&E (C). The tumour basement membrane surrounding the glands was positive for periodic acid-Schiff staining (D). The micrograph after counterstaining with Giemsa stain Melan A (E) and microphthalmia-associated transcription factor (F). The tumour had positive reactivity to the pancytokeratin OSCAR (G) and cytokeratin 7 (H) detected by performing alkaline phosphatase staining.

The tumour had grown endophytically, with invasion into the subepithelial stroma of the ciliary body (figure 2C). The tumour consisted of epithelial cells with moderate pleomorphic nuclei and prominent nucleoli. The tumour showed a nested, cord and glandular pattern. Periodic acid-Schiff (PAS) staining revealed that the tumour had a clearly glandular pattern with a prominent basement membrane surrounding the glands (figure 2D).

Immunohistochemical findings

Immunohistochemical studies showed that the tumour cells were diffusely and strongly positive for S100, Melan A and microphthalmia-associated transcription factor (MITF)

(figure 2E, F); were focally positive for EMA, showed no reactivity to cytokeratin CAM5.2; and were diffusely positive for OSCAR (figure 2G) and weakly positive for cytokeratin AE1/AE3 and cytokeratin 7 (figure 2H) HMB45 was positive in only the cells with brownish granules. The Ki-67 labelling index contributed to the diagnosis. A minimum of 1000 tumour nuclei were counted in this case. The Ki-67 index was 11%.

INVESTIGATIONS

Formalin-fixed paraffin-embedded specimens were cut into 4 µm thick sections. Deparaffinised sections were subjected to H&E and immunohistochemical staining. Immunohistochemical

staining was performed with the following primary antibodies: cytokeratin AE1/AE3, cytokeratin 7 (1:100; Dako, Glostrup, Denmark), cytokeratin OSCAR (1:100; Signet), cytokeratin CAM5.2 (1:20; Becton Dickinson Immunocytometry Systems, San Jose, California, USA), EMA (1:100; Dako), E29 (Dako), S100 (1:2000; rabbit polyclonal, Dako), HMB45 (1:10; Dako), Melan A (1:100; A103, Dako), MITF; 1:100; D5, Dako) and Ki-67 (1:100; MIB-1, Dako). Each section was exposed to 0.3% hydrogen peroxide for 15 min to block endogenous peroxidase activity. For staining, we used an automated stainer (Dako) according to the manufacturer's protocol. ChemMate EnVision HRP/DAB and G2 system AP kits (Dako) and counterstaining with giemsa were used for detection. Appropriate positive and negative controls were used for each antibody. Nuclear staining of the tumour cells was checked for positivity of S100, MITF, and Ki-67, and cytoplasmic staining was checked for positivity of cytokeratins, EMA, HMB45 and Melan A.

DIFFERENTIAL DIAGNOSIS

Epithelioid cell-type melanomas.

TREATMENT

Since the size of the lesion increased and MRI indicated 'adenoma' 3 months after presentation, the ciliary body was resected without eyeball enucleation.

OUTCOME AND FOLLOW-UP

No recurrence and metastasis was observed during a 9-month follow-up period.

DISCUSSION

In the present case, the tumour cells showed a high degree of melanogenesis, with pancytokeratin (OSCAR), CK7, Melan A, HMB45 and MITF immunopositivity. The pigmented epithelial cells of the iris, ciliary body and retina as well as melanocytes show melanogenesis. It is difficult to distinguish benign and malignant tumours of pigmented and non-pigmented ciliary epithelia from malignant melanoma of the ciliary body through clinical examination. Malignant melanoma has to be excluded via histological examination. Cytokeratin or EMA expression in either pigmented or non-pigmented neoplasms of the ciliary epithelium was reported to be focal or mild.³

Some cases of adenocarcinoma of the pigmented or non-pigmented ciliary epithelium have been reported to express S100, a well-known marker of melanocytic tumours.³ In our case, expression of Melan A, HMB45 and MITF, known markers of melanocytic tumours, were positive.⁴ Microphthalmia transcription factor (MITF) is essential in normal melanocyte development, and it controls the expression of pigmented cell phenotypes. The application of MITF and HMB45 as markers in the diagnosis of melanoma has been extensively studied. This is the first report of a pigmented ciliary adenocarcinoma being positive for MITF and HMB45. Therefore, comprehensive evaluation of parameters including morphology, imaging results and clinical information is required for proper diagnosis. The criterion used for the diagnosis and

differentiation of adenoma arising from the ciliary pigmented epithelium is local invasion to the iris, ciliary body stroma, anterior chamber angle and sclera.¹ In the present case, the tumour clearly invaded the ciliary body stroma around the vessels and showed moderate pleomorphism. In addition, the Ki-67 and mitotic indices might indicate malignant behaviour.

The prognosis of adenocarcinoma of the pigmented ciliary epithelium has not been elucidated. Although the tumours have been described as showing extraocular extension and metastasis to other organs in a few case reports, tumour relapse or metastasis after tumour resection or enucleation of the eye has not been reported.⁵ Adenocarcinoma of the pigmented ciliary epithelium seems to have a relatively good prognosis compared with malignant melanoma.

A pathologist who encounters a tumour arising from the ciliary body with evidence of melanogenesis should be attentive to the existence of epithelial features in order to differentiate adenocarcinoma of the pigmented epithelium from malignant melanoma.

Learning points

- ▶ Adenocarcinoma of the pigmented ciliary epithelium is an exceptionally rare malignant eye tumour.
- ▶ This tumour was positively immunostained for pancytokeratin (OSCAR), Melan-A, S-100, HMB45 and microphthalmia-associated transcription factor.
- ▶ Diagnosis of pigmented eye neoplasms requires comprehensive evaluation of many parameters including the morphology, MRI findings and immunohistochemical results.

Acknowledgements The authors are grateful to Dr Yukiko Aihara, Dr Miyuki Fujiwara, Dr Ryoji Kushima and Dr Akiko Maeshima for supporting this work and Ms Sachiko Miura and Ms Chizu Kina for their skilled technical assistance.

Contributors AS and TM designed the manuscript and made the diagnosis. AO made the pathological diagnosis and SS provided the clinical data.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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