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Incidental finding of double nodular microscopic hyperplasia versus adenoma of the retinal pigment epithelium in an eye eviscerated for phthisis bulbi

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Abstract

Neoplasms of the retinal pigment epithelium (RPE) are very rare and can clinically simulate choroidal melanoma. The clinical, histopathological and immunohistochemical features of incidental double pseudo-neoplastic proliferation of the RPE in an eviscerated eye for phthisis bulbi are reported. The differential diagnosis of RPE neoplasms and the utility of histopatological examination of eviscerated/enucleated eyes are discussed. ***Clin Ter 2010; 161(5):?-?***

Key words: *adenoma, hyperplasia, immunohistochemistry, phthisis bulbi, retinal pigment epithelium, RPE*

Introduction

Tumors of the retina especially adenocarcinoma of the retinal pigment epithelium (RPE) are extremely rare (1-3). The RPE can be involved in a spectrum of pseudo-neoplastic and neoplastic processes including reactive hyperplasia, congenital hypertrophy, combined hamartoma and, less commonly, adenoma (4).

In the majority of cases diagnosis of the lesions affecting the RPE is performed on clinical grounds, however, rarely they can represent a surprise upon histopathological examination of enucleated/eviscerated eyes (1).

Case Report

A 70 year old male was admitted to hospital for pain in the right eye since 4 months. 50 years previously he had had a facial trauma with penetrating injury to the right eye leading to immediate loss of vision. The general history was unremarkable.

Ocular examination showed a normal orbit with a subatrophic bulbi. Ocular adnexa were normal. Slit lamp examination revealed hyperemic conjunctiva, cloudy cornea, increased depth of the anterior chamber, residual iris tissue in the superior temporal area with irregular mydriasis and aphakia. Observation of the posterior segment with indirect biomicroscopy showed white fibrotic tissue of the vitreous-retina. Intraocular pressure was low. Ultrasound examination was not performed. Evisceration was carried out.

The eyeball was fixed in 4% phosphate-buffered formaldehyde and embedded in paraffin. Sections were cut at 5 µm and mounted on glass slids. Deparaffinized sections were stained with hematoxylin-eosin (H&E). For immunohistochemistry analysis 5 μm tissue sections from paraffin block were mounted on poly-L-lysine coated glass slides and deparaffinized. Antigen expression was determined using the avidin-biotin complex method. The following primary antibodies were used:

Mouse monoclonal antibodies (mAb) against pancytokeratin (MNF116, 1:50), cytokeratins (AE1/3, 1:50), cytokeratin (CAM 5.2, pre-diluted), HMB-45 (HMB-45, 1:50), melan-A (A103, 1:50), NSE (BBS/NC/V1-14, 1:100), NFP (2F11, 1:100), GFAP (6F2, 1:25), ki67 (Ki-S5, 1:40), p53 (DO7, 1:80) and rabbit polyclonal antibodies against S-100 protein (1:150).

All antibodies were purchased from Dako (Glostrup, Denmark) except for cyotokeratin CAM 5.2 obtained from Becton Dickinson (San Jose, CA). A section of tissue expressing the corresponding antigen, was used as a positive control for each antibody. Negative controls without the primary antibody were performed.

The normal structures of the eye were not recognizable on histopathological examination. There was extensive fibrosis, calcification and osseous metaplasia. Two small nodular proliferations, arising from the RPE were detectable (Fig. 1). The thickness of the lesions was 1 mm and 1.7 mm.

The lesions were composed of epithelioid cells with intracellular pigment, arranged in closely packed tubules and glandular structures. The cells, characterized by round vesicular nuclei and very prominent nucleoli, were embedded in abundant extracellular eosinophilic basement membrane-like material (Fig. 2). There was no cellular pleomorphism and necrosis. None of the lesions displayed mitosis.

Immunohistochemical analysis showed that the neoplastic cells were diffusely positive for cyotokeratin CAM 5.2 (Fig. 3) and focally positive for cytokeratins AE1/3 (data

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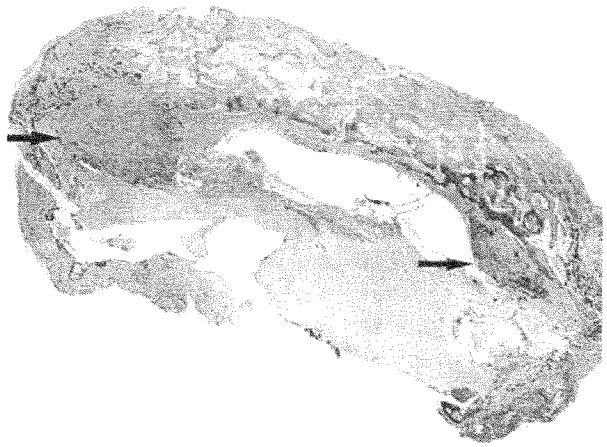

Fig. 1. At low magnification the normal structures of the eye cannot be identified. An extensive area of osseous metaplasia is present. The arrows indicate two small nodular proliferations originating from the RPE.

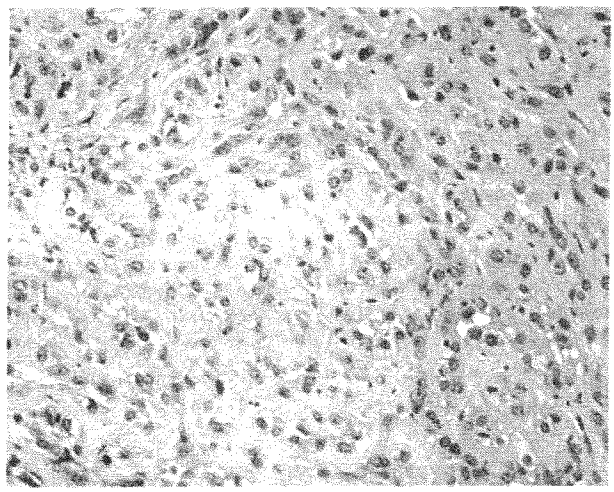

Fig. 2. At higher magnification the cells are characterized by round vesicular nuclei and prominent nucleoli. Note the conspicuous deposition of extracellular collagenous tissue.

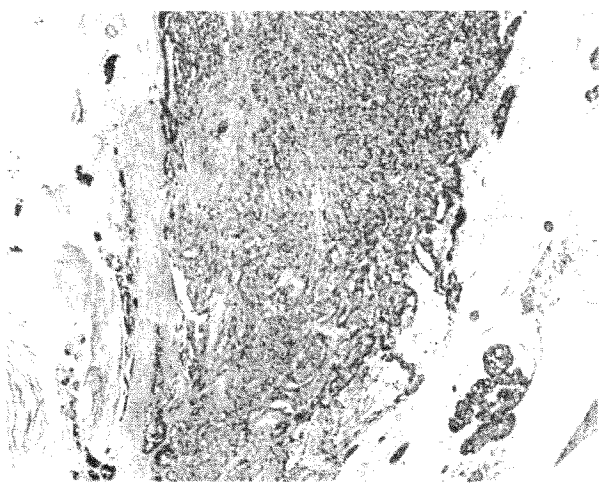

Fig. 3. Diffuse immunohistochemical cytoplasmic positivity for cytokeratin CAM 5.2.

not shown). Immunostaining for pancyotokeratins MNF116, S-100, HMB-45, Melan-A, NSE, GFAP, NFP, p53 and proliferative marker ki67 was negative.

Discussion

Adenomas and hyperplasia of the RPE are very rare (3-5) and represent a challenge for both clinicians and pathologists. For the formers they may simulate a choroidal malignant melanoma and for the latters the histological differential diagnosis between reactive nodular lesions and true neoplasms of the RPE may be very difficult. In our case the lack of cellular pleomorphism and mitotic figures was against the diagnosis of adenocarcinoma. The immunohistochemical findings were contrary to a melanotic neoplasm. The main differential diagnosis was between adenoma and nodular hyperplasia of the RPE. The criteria to distinguish these two lesions has been previously reported (6). Nodular hyperplasia of the RPE usually arise in long-standing, blind, damaged eyes by disease or injury. The histological demonstration of inflammation, massive scarring and osseous metaplasia indicates a reactive lesion of the RPE, whereas adenoma usually occurs in healthy eyes. However, there are also intermediate lesions which can not be histologically classified with certainty.

The most common motives for eye removal are recent or remote trauma, glaucoma, malignant melanoma, endophthalmitis, retinal detachment and pthisis bulbi. Over the past years there seems to be a decrease in the number of enucleations with respect to evisceration (2). The advantage of evisceration is the preservation of tissue, improved cosmetic aspect, better prosthesis mobility and reduced frequency of extrusion of the orbital implant and intracranial infection (7-9).

In a report on 285 histopathology results after enucleation/evisceration (2), three cases were diagnosed as metastatic carcinoma which was suspected preoperatively. However, in one eye removed for pain and phthisis, the diagnosis of adenocarcinoma was a surprise upon histological examination.

Histology is fundamental in cases where history or clinical examination lead to suspicion of intra-ocular tumor. In these cases enucleation permits thorough histopathologic examination of the intact globe and a section of the optic nerve for diagnostic determination of intraneural or extrascleral extension of ocular malignancy. In the case reported herein, histological diagnosis of nodular hyperplasia versus adenoma of the REP was made on an eye eviscerated for phthisis bulbi with no previous suspicion of intraocular tumor. In one study a 10 to 16% incidence of unsuspected intraocular malignancies in eviscerated eyes with opaque media was reported (10). However, the percentages may be higher with respect to more recent investigations due to currently available procedures such as ultrasound examination.

Routine ultrasound examination prior to evisceration or enucleation should be advocated as this is a non-invasive and simple test. Even though the microscopic size of the neoplasms in our case could have yielded doubtful results at routine ultrasound examination. In those cases where history, inadequate examination due to opaque ocular media

or surgical findings are unclear histological examination should be recommended. This analysis is helpful for both patient follow-up and the evaluation of the incidence of intraocular malignancies.

References

1. Saeed MU, Chang BY, Anand S, et al. Diagnostic surprise in an evisceration specimen. Orbit 2007; 26(2):129-31
2. Saeed MU, Chang BYP, Khandwala M, et al. Twenty year review of histological findings in enucleated/eviscerated eyes. J Clin Pathol 2006; 59:153-5
3. Heegaard S, Larsen JN, Fledelius HC, et al. Neoplasia versus hyperplasia of the retinal pigment epithelium. A comparison of two cases. Acta Ophthalmol Scand 2001; 79(6):626-33
4. Shields JA, Shields CL. Intraocular Tumors: A Text and Atlas. Philadelphia, Pa: WB Saunders Co 1992; 437-60
5. Garner A. Tumors of the retinalpigment epithelium. Br J Ophtalmol 1970; 54:715-23
6. Tso MO, Albert DM. Pathological condition of the retinal pigment epithelium. Neoplasms and nodular non-neoplastic lesions. Arch Ophthalmol 1972; 88(1):27-38
7. Dortzbach RK, Woog JJ. Choice of procedure. Enucleation, evisceration, or prosthetic fitting over globes. Ophthalmol 1985; 92:1249-55
8. Hansen AB, Petersen C, Heegaard S, et al. Review of 1028 bulbar eviscerations and enucleations. Changes in aetiology and frequency over a 20-year period. Acta Ophthalmol Scand 1999; 77:331-5
9. Genovois O, Millet P, Retout A, et al. Comparison after 10 years of two 100-patient cohorts operated on for eviscerations or enucleations. Eur J Ophthalmol 2004; 14:363-8
10. Green WR, Maumenee AE, Sanders TE, Smith ME. Sympathetic uveitis following evisceration. Trans Am Acad Ophthalmol Otolaryngol 1972; 76:625-44