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Case Report:

Adenoma of nonpigmented epithelium in ciliary body: literature review and case report*

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Abstract: Adenomas of the nonpigmented ciliary epithelium (NPCE) are often clinically indistinguishable from amelanotic malignant melanomas of the ciliary body or metastatic carcinomas. This paper reports a case study of a distinctive variant of adenoma of the NPCE, which clinically appears as epiretinal membrane in the macular region. Histopathologic studies have revealed this is an adenoma of the NPCE. Identification of this clinic feature is important because it will miss the diagnosis of the adenoma of the NPCE. In this case study, B-scan ultrasonography as well as computerized tomography (CT) has been used to provide help in diagnosing the ciliary body tumor. Because of their anterior location in the ciliary body, partial lamellar sclerouvectomy is an effective method of treatment.

Key words: Epiretinal membrane, Ciliary body, Uveal tumor, Adenoma
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INTRODUCTION

Adenoma of nonpigmented ciliary epithelium (NPCE) is an extremely rare benign ciliary body tumor. Since the first case described by Shields *et al*.(1983), over 20 cases of adenoma have been reported in the medical English literature. Acquired tumors of the ciliary body have displayed a wide spectrum of clinicopathologic features and biological behavior (Mansoor and Qureshi, 2004). Although it is a benign tumor, adenoma of the NPCE can cause severe local symptom, such as intra-ocular inflammation (Biswas *et al*., 1995; Shields *et al*., 1996), secondary cataract (Biswas *et al*., 1995; Elizalde *et al*., 2006; McGowan *et al*., 1991; Nakazawa *et al*., 2000; Shields *et al*., 1996), subluxation of the lens, secondary glaucoma, vitreous hemorrhage (Biswas *et al*., 1995), and neovascularization of the optic disk and cystoid macular edema (Suzuki *et al*., 2005). The clinical technical approach for diagnosis included slit lamp exanimation, gonioscopy, fluorescein angiography, ultrasonography and computerized tomography (CT). Local resection such as partial lamellar sclerouvectomy is an effective method to the treatment and to confirm the diagnosis. The eye will be enucleated because of the progressive enlargement with poor vision and uncontrolled secondary glaucoma.

In many cases, a definitive diagnosis of adenoma can only be achieved through histopathological studies. The cells of the tumor are arranged in linear bands, strands or cords that are aligned along, and separated by septa of extra-cellular matrix material. The immunohistochemical results were observed to be consistent with an origin from the NPCE: S-100, vimentin and cytokeratin are positive while the HMB45 antibody is negative (Mansoor and Qureshi, 2004).

In this report, a case of an adenoma of the NPCE in a 29-year-old Chinese male concomitant with unusual clinicopathological features as epiretinal membrane is reported. Epiretinal membrane is seen most often in people over 50 years of age. Occasion-

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ally, children and young adults may get an epiretinal membrane. To our knowledge, the epiretinal membrane concomitant with the adenoma of NPCE has not been reported before. The clinical finding of epiretinal membrane is accessed by ophthalmoscope and fluorescein angiography. Ultrasonography and CT investigation found the mass in ciliary body. Histopathological examination showed an adenoma of the NPCE.

CLINICAL SUMMARY

The patient, a 29-year-old Chinese male, had a 2-month history of blurred and distorted vision in his left eye at the time of referral for treatment. The patient had no prior medical history of ocular trauma or intraocular disorders. The best-corrected visual acuity of the patient was 0.04, and the intraocular pressure was 14 mmHg in the affected eye. Slit-lamp examination of the left eye revealed a clear anterior chamber, transparent lens, some flare and cells in the vitreous cavity. A small white mass was observed behind the iris at the 2 to 3 o'clock region when the pupil was fully dilated, marked as yellow-white epiretinal membrane in Fig.1. The tumor was evaluated using B-scan ultrasonography and CT images. On B-scan ultrasonography, the tumor was acoustically solid, had high internal reflectivity and abruptly elevated margin with a size of 4 mm×3 mm, as shown in Fig.2a. CT images showed a circular compact mass with a CT value of 251 Hu and a diameter of 4 mm, as shown in Fig.2b. After the patient's condition was diagnosed as ciliary body tumor, local resection of the tumor was performed for treatment. The tumor was then completely excised for pathological examination.

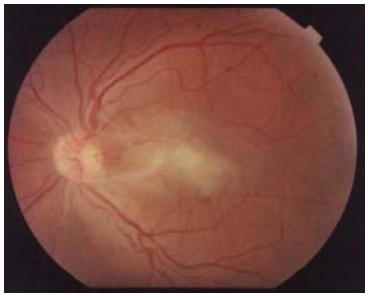
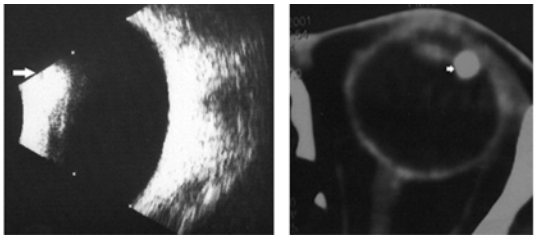


Fig.1 Fundus color photograph, a yellow-white epiretinal membrane was observed in the macula

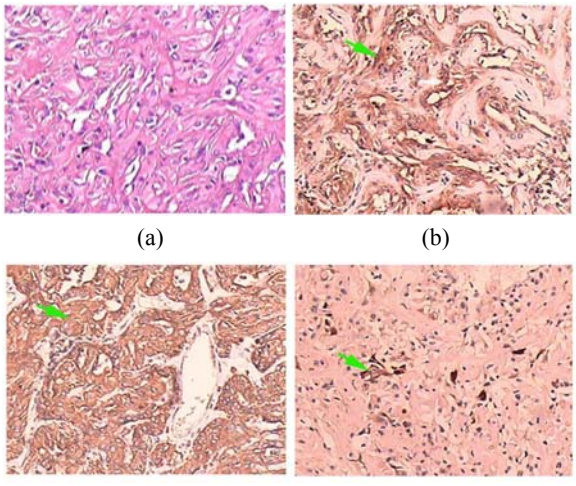


(a) (b)

Fig.2 (a) B-ultrasound inspection of left eye revealed a clear-boundary mass in the superotemporal with the size of 4 mm×3 mm; (b) CT examination of the left eye revealed a circular compact mass on ciliary body with the CT value of 251 Hu and the diameter of 4 mm

PATHOLOGICAL FINDINGS

Formalin-fixed and paraffin-embedded specimens of the tumor were stained by hematoxylin and eosin (HE) and subsequently examined using a microscope. On gross pathological examination, the tumor was amelanotic and showed an irregular surface. Histopathological examination showed the tumor was comprised primarily of cubic and polygonal cells with abundant eosinophilic cytoplasm, forming a combination of tubular and cordlike components (Fig.3a). Strong positive reaction to S-100 protein (Fig.3b) and vimentin (Fig.3c) was detected as well as mild positive immunoreactions to cytokeratin CK (AE1/AE3) (Fig.3d), while negative reaction to



(a) (b)

(c) (d)

Fig.3 Appearance under light microscopy of the tumor, stained with HE (a). Strong positive reaction to S-100 protein (b) and vimentin (c), mild positive immunoreactions to cytokeratin CK (AE1/AE3) (d) were observed

HMB45 was found in the tissue sample. Based on all these observations, the results of immunostaining suggested that NPCE should be the origin of the tumor, which was consistent with the results as reported by Shields *et al*.(1996). After local resection was performed, vitreous hemorrhage happened in the affected eye of the patient, who declined a proposal to take subsequent vitrectomy.

DISCUSSION AND CONCLUSION

Primary tumors of the NPCE are very rare. Generally, there are two classes of primary tumors of the NPCE: congenital and acquired adenoma. Acquired neoplasms of the NPCE include Fuchs adenoma, adenoma, and carcinoma of the NPCE (Mansoor and Qureshi, 2004). Acquired tumors of the ciliary body have a wide spectrum of clinicopathologic features and biological behavior. Most information about these has come from single case reports. Over 20 documented cases of acquired adenoma of the NPCE have been reported in the medical English literature. Adenomas are distinguished from adenocarcinoma of the NPCE by the absence of local infiltrative behavior and rare mitoses (Cursiefen *et al*., 1999). This tumor is mostly seen in adults, with ages ranging between 24 to 70 years, and without a sex predilection. Despite its being a benign tumor, adenoma of the NPCE can behave quite aggressively in local region, causing secondary cataract (80%), subluxation of the lens (40%), intra-ocular inflammation (40%), secondary glaucoma (15.2%), vitreous haemorrhage (15.2%), and neovascularization of the optic disk and cystoid macular edema (5.0%). The number in the bracket indicates the percentage of each case in the reported 20 cases. The tumors were almost predominantly not pigmented and were white to light tan in color (Shields *et al*., 1996). Histopathologically, the tumors showed considerable variation among patients. The cells comprising the tumor were arranged in linear bands, strands or cords that are aligned along (Grossniklaus and Lim, 1994) and separated by septa of extra-cellular matrix material. These septa are often quite prominent and typically stained positive with the periodic acid Schiff stain. Many cases of the NPCE adenoma contain pools of hyaluronidase-sensitive acid mucopolysaccharide (McGowan *et al*., 1991). The immunohistochemical results were consistent with an origin from the NPCE: S-100, vimentin and cytokeratin are positive while the HMB45 antibody is negative.

In the present case, we found that the age, sex, and histopathological findings are typical of adenoma of the NPCE. The B-scan ultrasonography and CT of the lesion clearly showed its location within the ciliary body. The histological and immunohistochemical findings in the present case are typical of the adenoma of the NPCE described by Mansoor and Qureshi (2004).

The described adenoma of the NPCE in this case study is very rare because it is concomitant with the epiretinal membrane. Epiretinal membranes involving the macular or perimacular regions can cause a reduction in vision, metamorphopsia, micropsia, or occasionally monocular diplopia in elderly patients. Epiretinal membrane usually occurs for unknown reasons, called idiopathic epiretinal membrane, but may be associated with certain eye problems such as: intraocular inflammation (Harada *et al*., 2006), diabetic retinopathy (Harada *et al*., 2004), posterior vitreous detachment (Johnson, 2005), retinal detachment (Council *et al*., 2005), and many others. The epiretinal membrane may be mostly developed secondary to the inflammation since flare and cells are detected in the vitreous cavity in the affected eye of this case. Tumor necrosis factor-alpha (TNF-α) and nuclear factor kappa B (NF-κB) have been implicated in a wide variety of diseases such as tumor and other inflammatory diseases (Sebban and Courtois, 2006; Szlosarek *et al*., 2006; Xanthoulea *et al*., 2004). Recently, Suzuki *et al*.(2005) reported that the increased level of vascular endothelial growth factor might contribute to the neovascularization of the optic disk and cystoid macular edema in a case with the adenoma of NPCE. These cytokines might play an important role in membrane growth in proliferative disorders (Harada *et al*., 2006).

In conclusion, adenoma of NPCE is rare. Acquired tumors of the ciliary body have distinctive clinical and histopathological characteristics that can help the diagnosis. Because the ciliary body tumor is often difficult to visualize clinically, it should be kept in mind that epiretinal membrane may be concomitant with ocular tumor, especially in young patients. Based on this study, B-scan ultrasonography and CT

may be used to assist diagnosis of ciliary body tumor. Because of their anterior location in the ciliary body, local resection is usually the treatment of choice.

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