Int J Clin Exp Pathol 2016;9(11):12008-12012
www.ijcep.com /ISSN:1936-2625/IJCEP0026596

Case Report

Adenoma of the non-pigmented epithelium of the ciliary body with smooth muscle differentiation: a unique case report

Li-Mei Sun, Qing-Fu Zhang, Na Tang, Xue-Shan Qiu

Department of Pathology, The First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang, China

Received February 24, 2016; Accepted May 21, 2016; Epub November 1, 2016; Published November 15, 2016

Abstract: Adenoma of the non-pigmented epithelium of the ciliary body (ANPCE) is a relatively uncommon lesion usually presenting in the non-pigmented epithelium of the ciliary body, which belongs to the neuroectodermal origin. Histologically, this tumor consisted of sheets, cords, and tubules occasionally forming glandular configurations. The cells of the tumor had abundant eosinophilic cytoplasm with round nuclei and moderately prominent nucleoli, and separated by septa of extracellular matrix material. Herein, we present a case of adenoma of the non-pigmented epithelium of the ciliary body in a 48 year-old Chinese male. The tumor was clinically diagnosed as an amelanotic melanoma. Histologically, the tumor was predominately composed of sheets, strips, and tubular components, the tumor cells were round or spindle shaped, with round nuclei and an abundant cytoplasm where no pigment existed. Tumor cell nests were surrounded by hyalinized stroma, showing positive immunostaining for Actin of smooth muscle Actin (SMA) in the tumor and negative staining for S-100. As the most common primary neoplasms in the ciliary body were amelanotic malignant melanomas and metastatic carcinomas, the correct diagnosis of ANPCE may be a hard work.

Keywords: Adenoma, non-pigmented epithelium, ciliary body, smooth muscle differentiation

Introduction

ANPCE is an extremely rare non-pigmented epithelial tumor first described by Shields in 1983 [1]. It is usually considered benign ciliary body tumor [2], although it can result in a number of subsequent disorders [3]. ANPCE can occur at any age, but usually in adulthood, ranging in age from 24 to 70 years (median, 45 years), and without a sex predilection. The tumor is arising from the ciliary body, white or gray-white. ANPCE is histologically characterized by cords and nests epithelioid cells in extensive original fiber stroma. Herein, we present a case of ANPCE in a 48-year-old Chinese male. The tumor was predominantly composed of the cords or nests highly differentiated epithelioid cells, with smooth muscle differentiation and negative staining for S-100. These unusual immunohistochemical findings could be a potential diagnostic pitfall.

Case presentation

Clinical history

A 48-year-old male referred to our hospital for complaining of blurred vision of his right eye of one month duration. There was no history of trauma, diabetes, or hypertension. Computed tomographic scan of the eye revealed a well circumscribed, solitary mass about 6 mm in the ciliary body of right eye. The tumor was clinically diagnosed as an amelanotic melanoma, and then a mass excision was performed in our hospital. At surgery, the mass was removed, and underwent diagnostic examination.

Materials and methods

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4-μm slides, deparaffinized in xylene, rehydrat-

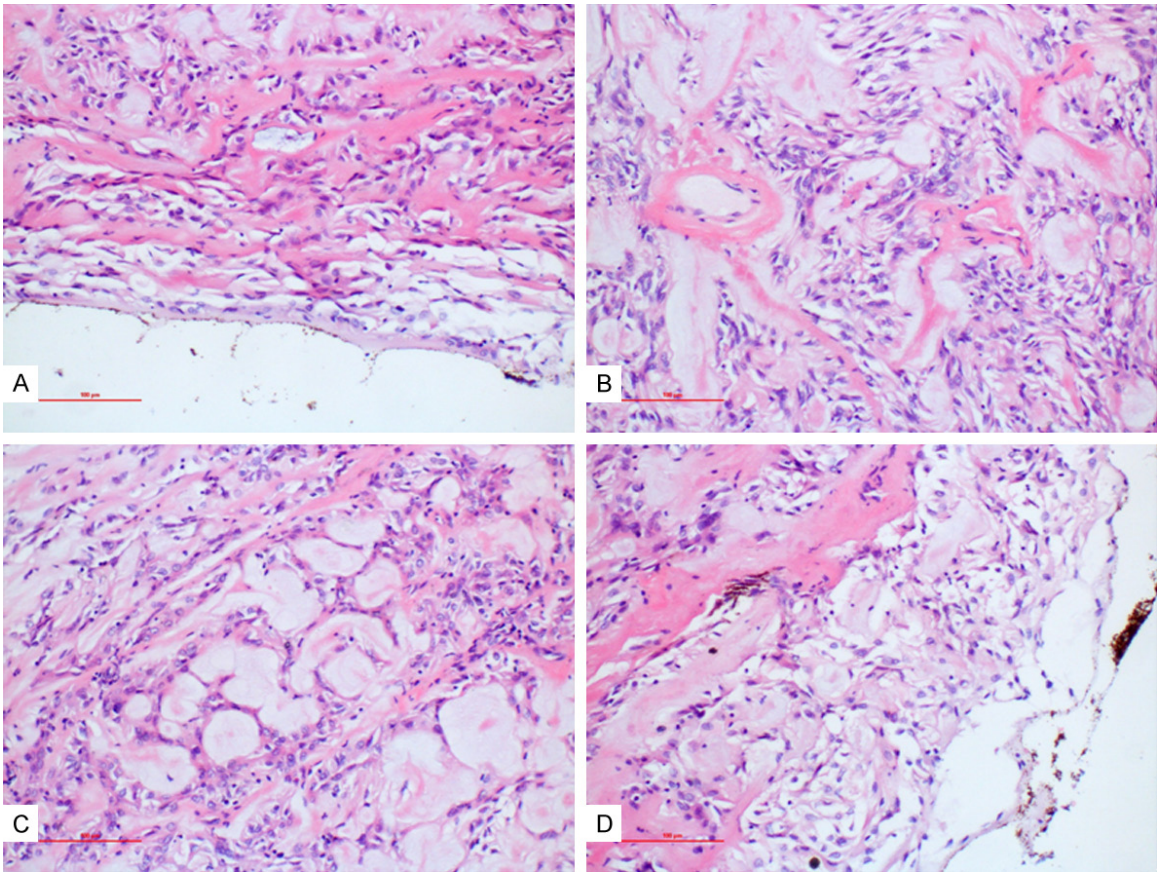

Figure 1. Morphological change of the tumor. A. The tumor was relatively well circumscribed. B. Numerous cuboidal epithelial cells were arranged into adenoid or cribriform patterns. C. The spindle cells cuboidal epithelial cells had no cellular atypia. D. The periphery may be the remaining melanin.

ed with graded alcohols, and immunostained with the following antibodies: Cytokeratin (pan), CD68, Vimentin, CD34, Desmin, Actin (SMA), S-100, melan A, HMB-45 and Ki67. Sections were stained with a streptavidin-peroxidase system (KIT-9720, Ultrasensitive TM S-P, MaiXin, China). The chromogen used was diaminobenzidine tetrahydrochloride substrate (DAB kit, MaiXin, China), slightly counterstained with hematoxylin, dehydrated and mounted. For the negative controls, the primary antibody was replaced with PBS.

Results

Gross features

Grossly, the mass was amelanotic and showed an irregular surface, was approximately 6.0×6.0×6.0 mm, and was well circumscribed. The cut face of the tumor was firm and grey-white in color.

Microscopic features

Histologically: The tumor was relatively well defined (**Figure 1A**). The tumor was predominantly composed of abundant round, polygonal, or spindle shaped cells. The cells were diffusely arranged into a variable combination of solid, sheets, strips, and some cuboidal epithelial cells were arranged into adenoid or cribriform patterns with little stroma (**Figure 1B**). The cells had no marked cellular atypia, with round or fusiform bland nuclei and an abundant cytoplasm where no pigment existed (**Figure 1C**). Mitoses were rare. In focal area of the tumor, the classic histologic structure, the cords or nests tumor cells with intracytoplasmic vacuoles in extensive myxohyaline stroma could be seen. The periphery may be the remaining melanin (**Figure 1D**).

Immunohistochemistry: Immunohistochemical staining showed that the epithelioid cells were

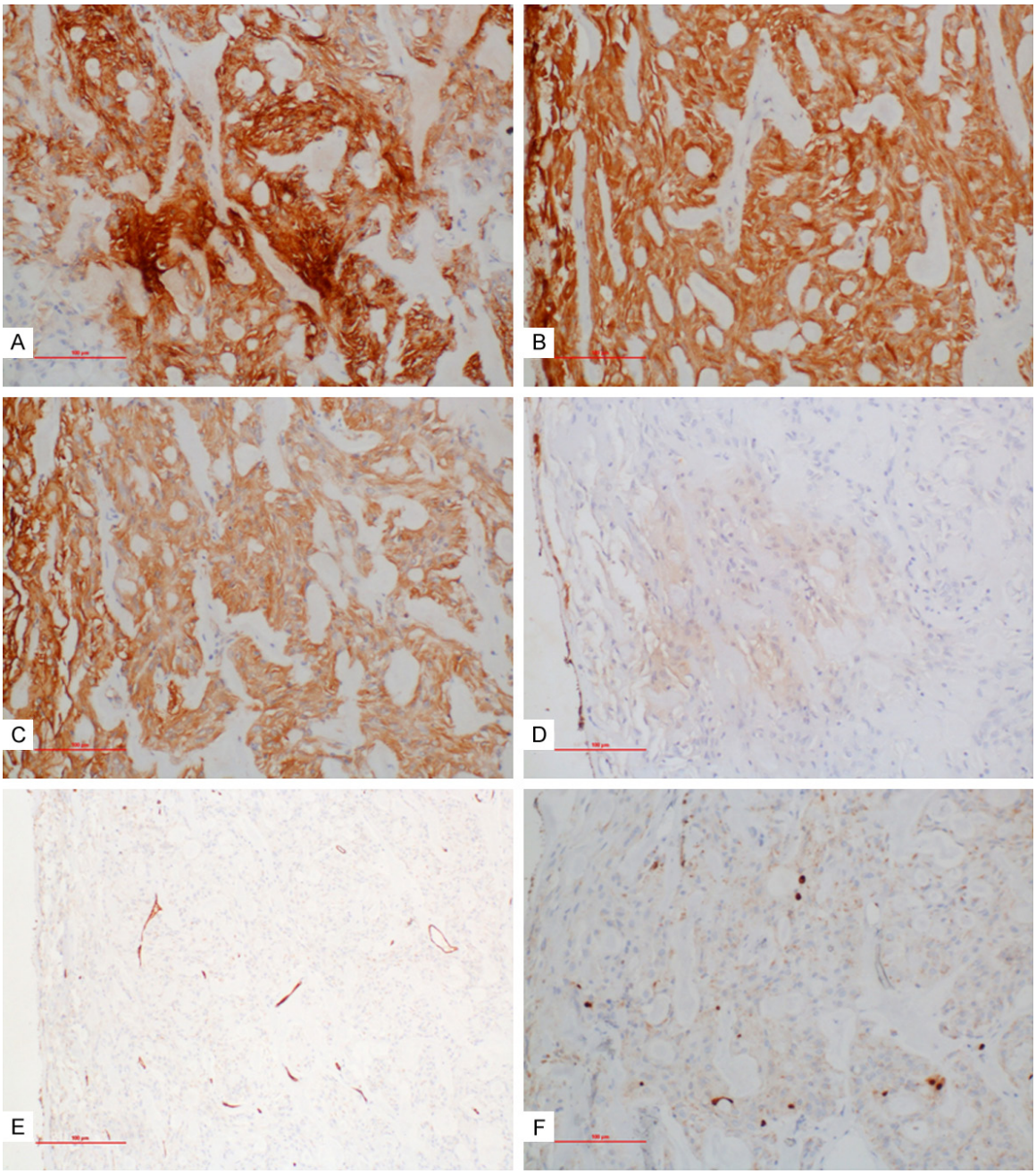

Figure 2. Immunohistochemical staining of the tumor. A. Diffuse and strong expression of Actin (SMA) could be seen in the cuboidal epithelial cells. B. The cuboidal epithelial cells were also positive for CK (pan). C. The cuboidal epithelial cells were also positive for Vimintin. D. The tumor cells were negative for S-100. E. The tumor cells were negative for CD34 in contrast to the positive expression of CD34 in normal blood vessel. F. Ki67 proliferative index was approximately 3%.

diffusely positive for Actin (SMA) (**Figure 2A**), Cytokeratin (pan) (**Figure 2B**), Vimentin (**Figure 2C**) and, negative for CD68, Desmin, GFAP, S-100 (**Figure 2D**), CD34 (**Figure 2E**), melan A and HMB-45. Ki67 (**Figure 2F**) index was approximately 2%. According to the morphological and immunohistochemical findings, the tumor was diagnosed as an adenoma of the non-pigmented epithelium of the ciliary body.

Discussion

Adenoma of the non-pigmented epithelium of the ciliary body (ANPCE) is a relatively uncom-

mon lesion which is considered a benign tumor. ANPCE can occur at any age, but usually in adulthood, with an average age of 45 years old, and without a sex predilection. The tumor is located in the ciliary body, white or gray-white, and only few cases are reported [4-11]. Histologically, ANPCE is characterized by cuboidal or columnar structure of non-pigmented epithelium. Tumor is arranged predominantly in a tubular and papillary configuration. The intervening areas are composed of mucoid fibrillary material. The tumor cells are quite bland, and show light atypia. Mitoses are rare. Usually, Strong positive reaction to S-100 protein and vimentin was detected as well as mild positive immunoreactions to Cytokeratin (pan) (AE1/AE3), while negative reaction to HMB45 was found in the tissue sample. Based on all these observations, the results of immunostaining suggested that nonpigmented ciliary epithelium (NPCE) should be the origin of the tumor, which was consistent with the results as reported by Shields et al [12] and Chen et al [13]. Our reported case show strong positive reaction to Actin (SMA), while negative reaction to S-100 was found.

The positive immunoreactivity for Actin (SMA) was puzzling. Actin (SMA) is thought to be specific for muscle cells, especially smooth muscle cells. But in our case we could not observe the phenotype of smooth muscle cells, such as short and spindle- or ovoid-shaped neoplastic cells, cigar shaped nuclei, fine nuclear chromatin and fibrillary cytoplasmic processes. Recent studies have demonstrated that the adult human ciliary epithelium contains progenitor cells with properties of smooth muscle stem cells which express Actin (SMA) and have the potential to proliferate and differentiate into smooth muscle cells [14, 15]. Diffuse expression of Actin (SMA) may be largely attributed to the muscle progenitor cells in the ciliary epithelium. And, further follow up should be made to investigate its significance. So we thought it might be an ANPCE with smooth muscle differentiation instead of ciliary body leiomyoma as reported by Shields JA et al [14] and Pecorella I et al [15]. But the significance of positive of Actin (SMA) is still unclear, further studies with larger patient population should be made to investigate its significance. ANPCE is extremely rare and, despite its amelanotic nature, may be mistaken for amelanotic malignant melanoma due to the most common site of melanomas in the ciliary body. But our reported case is not amelanotic malignant melanoma, because the negative expression of HMB45 and Melan-A.

In addition, the differential diagnosis includes some other tumors, such as: (1) Adenocarcinoma of the ciliary non-pigmented epithelium: adenocarcinoma is distinguished from adenoma of the NPCE by the abundant of local infiltrative behavior and rich mitoses. (2) Malignant melanoma: is located external to the ciliary pigment epithelium and therefore has a pigmented appearance. Tumor cells have obvious atypia. HMB-45 stains were positive. (3) Fuchs adenoma, benign hyperplasia of ciliary epithelium, is most common in the elderly. (4) Adenoma of the ciliary pigmented epithelium: it is usually deeply pigmented and more common in adults. (5) Leiomyoma of the ciliary body is more common in female. Immunohistochemical examination of muscle markers shows a positive reaction for leiomyoma. (6) Schwannoma of the ciliary body: Pathological features of schwannomas show Antoni A and B type that allows it to be readily differentiated from ANPCE. (7) Metastatic carcinoma: metastatic masses grow faster, and often occur in patients with a history of primary cancer.

Conclusion

Because of the exceptional rarity, the significance of the positive of Actin (SMA) in ANPCE is still unclear. We reported a case of ANPCE positive for Actin (SMA) and negative for S-100. This unusual immunohistochemical staining might result in a great pitfall in diagnosing epithelioid leiomyoma. It is important to use a set of antibodies, in order to make the correct diagnosis.

Acknowledgements

This work was supported by the Program for Liaoning Innovative Research Team in University (No: LC2015029), the Natural Science Foundation of Liaoning Province of China (No: L2015598), and the Program of Science and Technology Department of Liaoning Province (No: 2013225021).

Disclosure of conflict of interest

None.

Authors' contribution

SLM participated in the histopathological evaluation, performed the literature review, acquired photomicrographs and drafted the manuscript. TN carried out the immunohistochemical stains evaluation. ZQF conceived and designed the study. QXS gave the final histopathological diagnosis and revised the manuscript. All the authors read and approved the final manuscript.

Address correspondence to: Xue-Shan Qiu, Department of Pathology, The First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang 110001, China. E-mail: xsqiu@mail.cmu.edu.cn

References

[1] Shields JA, Augsburger JJ, Wallar PH, Shah HG. Adenoma of the nonpigmented epithelium of the ciliary body. Ophthalmology 1983; 90: 1528-30.

[2] Yan J, Liu X, Zhang P, Li Y. Acquired adenoma of the nonpigmented ciliary epithelium: analysis of five cases. Graefes Arch Clin Exp Ophthalmol 2015; 253: 637-44.

[3] McGowan HD, Simpson ER, Hunter WS, Pavlin CJ, Tanzer H. Adenoma of the nonpigmented epithelium of the ciliary body. Can J Ophthalmol 1991; 26: 328-33.

[4] Rennie IG, Parsons MA, Palmer CA. Congenital adenoma of the iris and ciliary body: light and electron microscopic observations. Br J Ophthalmol 1992; 76: 563-6.

[5] Grossniklaus HE, Lim JI. Adenoma of the nonpigmented ciliary epithelium. Retina 1994; 14: 452-6.

[6] Laver NV, Rubinfeld RS, Baum M, de Brito PA. Cytomorphology of a mixed pigmented/nonpigmented pleomorphic adenoma of the ciliary body: a diagnostic pitfall in the evaluation of intraocular tumors. Diagn Cytopathol 1996; 14: 259-62.

[7] Murphy MF, Johnston PB, Lyness RW. Adenoma of the non-pigmented epithelium of the ciliary body. Eye (Lond) 1997; 11: 419-20.

[8] Nakazawa T, Abe T, Sato Y, Yuda F, Omura M, Tamai M. Magnetic resonance imaging of a non-pigmented adenoma of the ciliary epithelium. Acta Ophthalmol Scand 2000; 78: 470-3.

[9] Mansoor S, Qureshi A. Ciliary body adenoma of non-pigmented epithelium. J Clin Pathol 2004; 57: 997-8.

[10] Elizalde J, Ubia S, Barraquer RI. Adenoma of the nonpigmented ciliary epithelium. Eur J Ophthalmol 2006; 16: 630-3.

[11] Papastefanou VP, Cohen VM. Ciliary-body adenoma of the non-pigmented epithelium with rubeosis iridis treated with plaque brachytherapy and bevacizumab. Eye (Lond) 2012; 26: 1388-90.

[12] Shields JA, Eagle RC Jr, Shields CL, De Potter P. Acquired neoplasms of the nonpigmented ciliary epithelium (adenoma and adenocarcinoma). Ophthalmology 1996; 103: 2007-16.

[13] Chen ZQ, Fang XY. Adenoma of nonpigmented epithelium in ciliary body: literature review and case report. J Zhejiang Univ Sci B 2007; 8: 612-615.

[14] Shields JA, Eagle RC Jr, Shields CL. Adenoma of nonpigmented ciliary epithelium with smooth muscle differentiation. Arch Ophthalmol 1999; 117: 117-9.

[15] Pecorella I, Ciocci L, Modesti M, Appolloni R. Adenoma of the non-pigmented ciliary epithelium: a rare intraocular tumor with unusual immunohistochemical findings. Pathol Res Pract 2009; 205: 870-5.