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Occurrence of trichoepithelioma in a cat: Histopathologic and immunohistochemical study

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KEYWORDS

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ABSTRACT

Trichoepitheliomas are benign follicular appendage tumors with differentiation to all three segments of the hair follicle. A 2 years old female domestic short hair cat presented with a mass on the tail. The mass was surgically excised and for histopathologic and immunohistochemical studies, was sent to Department of Pathology. Histologically, the tumor was encapsulated and consisted of many islands of follicular epithelium and also cysts structures which varied in size and shape. The cells of epithelium islands were round to oval and had variable amounts of slightly, eosinophilic cytoplasm and euchromatic nuclei. The cystic structures were lined by a complex layer of squamous epithelium. Often, cells under went an abrupt transition between basal layers and keratinization without the development of a granular cell layer. No tendency of malignancy was seen in this case. According to mentioned characteristics, trichoepithelioma was diagnosed. By immunohistochemical study it was confirmed that this tumor had epithelial origin because squamous tumor cells reacted with the pan-cytokeratin antibody. The expression of β-catenin was predominately cytoplasmic and also together with numerous positive nuclei but membranous expression was inconsistenet. Distribution of neoplastic cells with β-catenin expression was more than 75% and labeling intensity was strong in both cytoplasm and nuclei. According to author's knowledge, this is the first report of trichoepithelioma in cat in Iran and also investigation of β-catenin expression in feline trichoepithelioma in veterinary literature.

1. Introduction

Trichoepitheliomas (TEs) are benign follicular appendage tumors with differentiation to all three segments of the hair follicle (the infundibulum, isthmus, and the inferior segment). In these tumors, incomplete or abortive trichogenesis occurs[1]. These tumors generally occur in older animals[2]. TEs include approximately 80% of hair follicle tumors in domestic dogs, especially golden retrievers, basset hounds and German shepherds[2]. In domestic felids, TEs account for less than 1% of the reported hair follicle tumors[2].

In humans, spontaneous trichoepitheliomas are uncommon. They present in two clinical forms: solitary (non-hereditary) and multiple (autosomal-dominant) trichoepithelioma[1]. In human being, solitary trichoepithelioma of more than 2 cm in diameter are named giant solitary trichoepithelioma[1]. In dogs and cats, spontaneous trichoepitheliomas are also uncommon lesions that present as solitary tumors, although multiple tumors may happen rarely[1].

β-catenin is a protein encoded by the *CTNNB1* oncogene and is involved in cell-junctions and cytoskeletal dynamics with signaling pathways affecting morphogenesis, tissue homeostasis, and intercellular communication within tissues[3,4]. It has been shown that differentiation of the hair follicle is regulated and linked by β-catenin that initiate its development[5]. With immunohistochemical studies, membrane labeling of β-catenin identified in adult inter follicular epidermis (IFE), outer root sheath (ORS), inner root sheath (IRS) of hair follicles and also in the epithelial cells of adnexal glands[6,7].

In skin tissue, the Wnt/β-catenin pathway has a key role in different processes like cellular proliferation, regulation of tissue homeostasis and determination of cellular polarity. In addition, it is a critical element of epidermal stem cell maintenance and one of the central signaling pathways for epidermal differentiation and lineage selection[7,8]. Studies showed decreased and inconsistent membrane expression of β-catenin can be used as a negative prognostic factor in progression of malignant tumors[8]. Mutations of the *CTNNB1* oncogene, and/or genes encoding molecules of its degrading

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complex, are able to induce β-catenin accumulation in the cytoplasm and translocation into the nucleus with stimulation of cellular proliferation[8]. Several studies have suggested *CTNNB1* mutations occur in some human and canine follicular tumors such as trichoepithelioma and pilomatricoma and it means β-catenin can contribute to the tumorigenesis of these neoplasms[8].

According to author's knowledge, this is the first report of trichoepithelioma in cat in Iran and also investigation of β-catenin expression in feline trichoepithelioma in veterinary literature.

2. Case report

A 2 years old female domestic short hair cat presented with a mass on the tail. According to the statement of owner the growth of mass was started about a year ago. The overlying skin was sparsely haired. Clinical examination revealed the mass was firmly attached to the skin but it moved over the underlying tissues. The mass was surgically excised and for histopathologic and immunohistochemical studies, was sent to Department of Pathology. Sample was fixed in 10% (v/v) neutral buffered formalin, dehydrated, embedded in paraffin, 4-μm-thick section was cut from block and stained with hematoxylin and eosin. For immunohistochemical study, Sections were dewaxed and rehydrated. Heat-induced epitope retrieval was performed by immersion in boiling citrate buffer pH 6.0 for 2 min after reaching maximum pressure in a pressure cooker. Endogenous peroxidase was quenched by immersion in H_2O_2 3% in methanol for 10 min. Slides were then incubated in a moist chamber in a room temperature with a Monoclonal Mouse Anti-Human Cytokeratin (AE1/AE3; clone AE1AE3, Dako, Denmark) (1:80) and Anti β-catenin (Rabbit polyclonal antibody; clone H-102, Santa Cruz Biotechnology, Germany) (1:200) for 1.5 h. Secondary detection was by means of the Polyclonal Goat Anti-Mouse and biotinylated Goat Anti-Rabbit immunoglobulin. Positive labeling was 'visualized' by incubation with 3, 3′-diaminobenzidine (Dako, Denmark) and H_2O_2 for up to 7 min at room temperature and the section was then counterstained with haematoxylin, dehydrated and mounted.

In gross, the tumor was multi-lobulated and it was 0.6 cm×3.0 cm×0.2 cm. The cut surface was gray-white and some cavernous structures were seen.

Histologically, the tumor was encapsulated and consisted of many islands of follicular epithelium and also cysts structures which varied in size and shape (Figure 1). The cells of epithelium islands were round to oval and had variable amounts of slightly, eosinophilic cytoplasm and euchromatic nuclei. The cystic structures were lined by a complex layer of squamous epithelium (Figure 2). Cells often underwent an abrupt transition between basal layers and keratinization without the development of a granular cell layer. The centers of these structures were filled by lamellar or amorphous keratin and small amounts of melanin pigment. Pyknotic nuclear were present in the keratinaceous central mass in some cysts. Abortive attempts at trichogenesis within the cyst wall were occured between cysts and islands, moderate amounts of loose connective tissue were existed. The mitotic activity was 3-5 mitosis per 10 HPF and nuclear pleomorphism was slight. No tendency of malignancy was seen in this case. According to mentioned characteristics, trichoepithelioma was diagnosed.

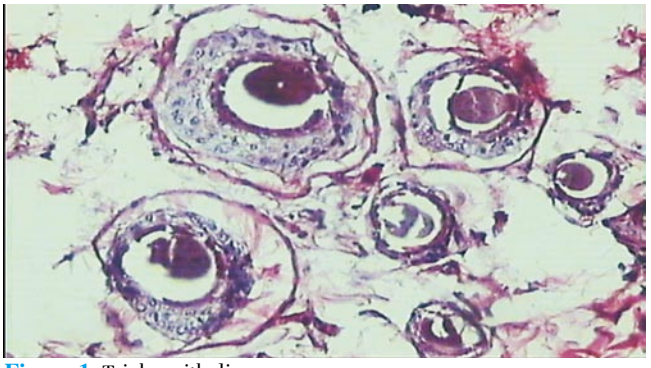

Figure 1. Trichoepithelioma.
Islands of follicular epithelium with abrupt and gradual keratinization (hematoxylin and eosin ×100).

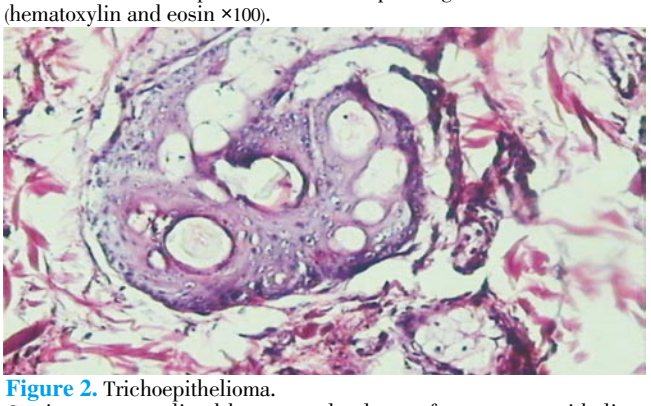

Figure 2. Trichoepithelioma.
Cystic structures lined by a complex layer of squamous epithelium (hematoxylin and eosin ×100).

By Immunohistochemical study it was confirmed that this tumor had epithelial origin because squamous tumor cells reacted with the pan-cytokeratin antibody. The expression of β-catenin was predominately cytoplasmic and also together with numerous positive nuclei but membranous expression was inconsistent. Distribution of neoplastic cells with β-catenin expression was more than 75% and labeling intensity was strong in both cytoplasm and nuclei (Figures 3 and 4).

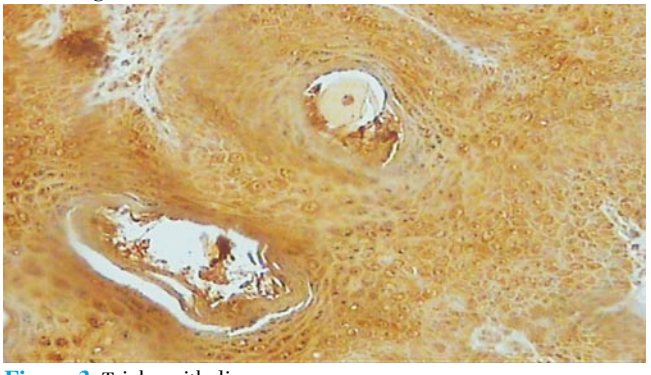

Figure 3. Trichoepithelioma.
Strong expression of β-catenin in both cytoplasm and nuclei (IHC ×100).

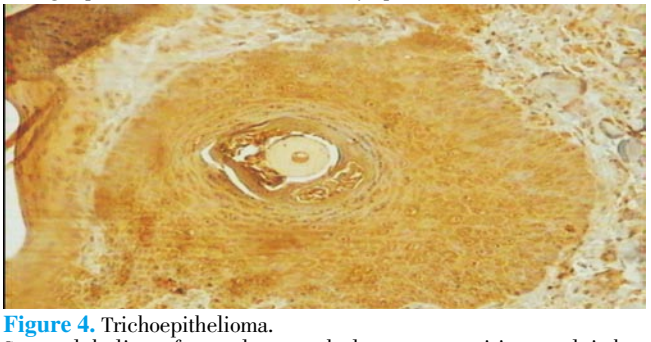

Figure 4. Trichoepithelioma.
Strong labeling of cytoplasm and also many positive nuclei that reacted with β-catenin antibody (IHC×100).

3. Discussion

Trichoepitheliomas are benign follicular tumors that composed of basaloid cells with follicular differentiation. They occur anywhere on the body with a slight preference for the back. It is an uncommon neoplasm in both human and domestic animal beings[1-9].

Differentials for TEs contain pilomatrixoma, tricholemmoma and trichofolliculoma[8]. But each of these tumors is differentiated based on the follicular structure affected. In present case, tumor cells originated from the primitive hair follicle and also occasionally with development of the basal layer, resulting in rapid keratinization without differentiation of granular cell layer. Follicular cysts must be differentiated from TEs by a lack of neoplastic follicular cells and their solitary occurrence[2].

Benign skin appendage tumors come from pluripotent cells, which differentiate towards hair, sebaceous gland or apocrine/eccrine glands. In some instances, primary epidermal germ cells and pluripotent cells differentiate in more than one direction[10].

Although TEs in domestic dogs are commonly ulcerated, in this case that occurred in cat, no ulcerative lesions were observed. Treatment of TEs is surgical excision and also no local recurrence or metastasis has been observed in domestic species[2].

The present study has demonstrated, for the first time in veterinary literature, the immunohistochemical expression of β-catenin in trichoepithelioma in cat. Bongiovanni *et al*. showed both canine epidermal and follicular tumors had a pattern of β-catenin expression similar to that reported in human counterparts[5,11-13]. Studies in human cutaneous follicular tumours showed that mutations in β-catenin gene related to their tumorigenesis[7,11,14,15]. Pervious studies demonstrated more than 75% of human pilomatricomas mutation of the *CTNNB1* gene, associated with a nuclear localization of the encoded molecules and this is reported in pilomatrical carcinoma as well as the benign forms of the tumor[7-11]. Furthermore, according to some authors in human studies, *CTNNB1* mutations are specic to tumors with matrical differentiation[7]. Also, a canine *CTNNB1* mutation was showed by Bongiovanni *et al*. In mentined research, numerous labelled nuclei were found in both pilomatricomas and the areas of matrical differentiation of trichoepitheliomas. In the present study, we observed cytoplasmic and nucleolus expression of this marker in feline tricoepithelioma that these findings were in agreement with human and canine studies. Bongiovanni *et al*. believed nuclear labeling, which is considered a hallmark of activation of the Wnt/β-catenin signaling pathway and was observed in canine follicular tumors, appears not to be specific to malignant tumors and suggests a possible mutation of canine *CTNBB1* gene. This result was similar to our finding in feline trichoepithelioma.

To conclude this paper, it reports occurrence of a trichoepithelioma in a cat and expression of β-catenin in this tumor, however, for better understand of the role of this molecule in skin tumors of cats, further studies should be performed.

Conflict of interest statement

We declare that we have no conflict of interest.

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