

Adenocarcinoma of Meibomian Glands and Moll Glands in the Eyelid of Canine

Dong-wei Yuan, Moon-Jung Goo, Hai-jie Yang, Il-Hwa Hong, Mi-Ran Ki, Jin-Kyu Park,
Hye-Rim Lee, Sung-Eun Yoo¹ and Kyu-Shik Jeong*

Department of Pathology, College of Veterinary Medicine, Kyungpook National University, Daegu 702-701, Republic of Korea

¹*Korea Research Institute of Chemical Technology, Daejeon, Republic of Korea*

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A 4-year-old female beagle with progressive exophthalmos and which had a neoplastic mass with diameter of 1.4 cm in the left lower ocular adnexa. Histologically, the mass was composed of hyperplastic lobules and tubular structures separated by fibrous septum. The well differentiated sebaceous gland forming various sized lobules, and infiltration of mast cells and mononuclear inflammatory cells were observed. Apical decapitation secretion of these tubular structures with basophilic materials in their lumen showed mild sebaceous gland metaplasia. Immunohistochemical studying, cell groups were positive in α -SMA and vimentin. The primary tumor was diagnosed as adenocarcinoma originated from moll gland and meibomian gland of the eyelid, and the infiltrating intraocular neoplasm was diagnosed as a malignant mixed tumor.

Key words : Adenocarcinoma, dog, eyelid, meibomian gland moll gland

Introduction

The eyelids are folds of tissue lined by skin anteriorly and palpebral conjunctiva posteriorly [5]. In dogs, eyelid neoplasms are the most frequent group of ophthalmic neoplasms. However, meibomian gland adenoma, benign melanoma, and papilloma are the most frequently observed eyelid tumors, representing 88% of eyelid neoplasms, and malignant eyelid neoplasia is rare in the dog but when diagnosed, mast cell tumor, sebaceous gland adenocarcinoma, basal cell carcinoma, melanoma, squamous cell carcinoma, hemangiosarcoma, and myoblastoma, fibrosarcoma are the cell types reported, representing 8.2% of eyelid tumors [13], but metastasis of eyelid tumors was not observed [3].

The glands of eyelid consist of sebaceous glands such as meibomian (tarsal) and zeis glands that opens to hair follicles and moll glands that have modified sweat gland characteristics [5]. Meibomian glands are found on the tarsal plate and are responsible for the formation of oily layer over the thin film of tear [8]. The meibomian glands (or tarsal glands) are a special kind of sebaceous glands at the rim of the eyelids, adenocarcinoma of the meibomian glands is a rare tumor of the eyelid [10], with atypical

glandular features, which appear initially as a chalazion formation and then invades the neighbouring tissues [11]. Modified sweat glands have apocrine secretion and leave their secretions inside the eyelash follicles, and modified sweat gland tumors in dogs occur at any site, and represent 2.2% of canine skin tumors [1]. There are few published reports of modified sweat gland tumors of the eyelid in dogs.

In the veterinary literature, there is no case report about the coexistence of malignant tumors of both glands. This paper describes a distinct clinical condition in a 4-year-old, female beagle dog which is characterized by malignant mixed adenocarcinoma which has a presumed origin from meibomian glands, but accessory modified sweat gland and the third eyelid.

Materials and Methods

A 4-year-old, female beagle dog was taken to hospital with cherry eye, clinical presentation included a mass of ocular adnexa extended from the subconjunctiva to the lower eyelid of the left eye which resulted in swollen conjunctiva and pyogenesis secretion. The mass protrusion the third eyelid and connected with the left lower eyelid, like an oval tumor formation as the diameter about 1.4 cm, with gray reddish color and whitish lobulated cut surface were observed (Fig. 1). The mass on the eyelid was surgically

*Corresponding author

Tel : +82-53-950-5975, Fax : +82-53-950-5955

E-mail : jeongks@knu.ac.kr

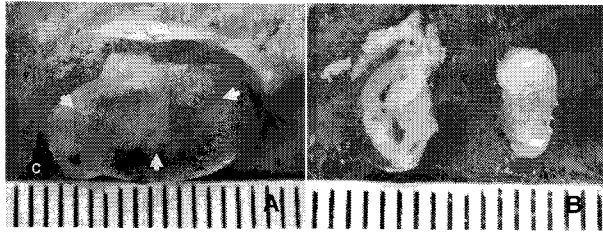


Fig. 1. Eye; dog. **A**, In sagittal section, the neoplastic mass (arrows) extends from the subconjunctiva to the third eyelid. The globe is filled with neoplastic tissue. C=cornea. **B**, The cut section of the extracted lower eyelid tumor mass, the tumor mass had whitish lobulated cut surface.

excised under local anesthesia. Using an operating microscope, the mass and the free margin of the third eyelid were totally excised. The surgical wound was left to heal by second intention. The eye was treated postsurgically with choramphenicol sulfonamide eye drops solution TID to prevent infection.

The biopsy was fixed with 10% neutral buffered formalin solution, and it was embedded in paraffin following the routine processing. 5-micron-thick sections obtained from the paraffin blocks were stained with hematoxylin-eosin (HE) and 2.5% toluidine blue, and then examined under light microscope. Additional sections were also obtained to evaluate immunohistochemical staining with avidine biotin peroxidase complex (ABC) method using monoclonal antibodies such as mouse anti-pancytokeratin (Dako), mouse anti-alpha smooth muscle actin (α -SMA) (Novocastra) and anti-vimentin (Dako).

Results

In the microscopic examination, superficial pyogranuloma of conjunctiva was founded; the tissue was fairly well-differentiated, hyperplastic lobules of acinar and tubular structures separating by fibrous septa, and characteristically invasive growth (Fig. 2A). The neoplastic glandular tissue was found interspersed with fully differentiated and normally organized nonneoplastic glandular tissue, well differentiated tubules and acinus were lined with well differentiated cuboidal to columnar epithelial cells having abundant cytoplasm with oval to round nuclei (Fig. 2B). Apical decapitation secretion of these tubular structures with basophilic materials in their lumen showed mild sebaceous gland metaplasia (Fig. 2C), well differentiated sebaceous gland forming various sized lobules having vacuolar

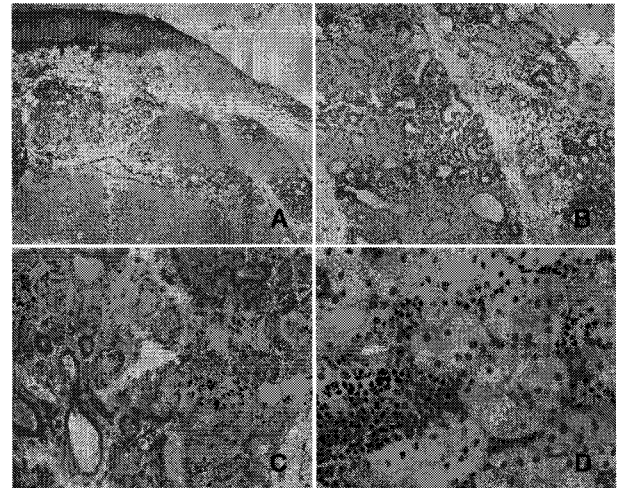


Fig. 2. Light micrographs of the eyelid mass. **A**, Superficial pyogranuloma of conjunctiva, hyperplastic lobules of acinar and tubular structures separated by fibrous septa and invasive growth. H&E stain, $\times 50$. **B**, Well differentiated tubules and acinus was lined with well differentiated cuboidal to columnar epithelial cells. H&E stain, $\times 100$. **C**, Tubular structures with basophilic materials in their lumen and some of these tubular structures showed mild sebaceous gland metaplasia. H&E stain, $\times 100$. **D**, Well differentiated sebaceous gland forming various sized lobules and infiltration of mononuclear inflammatory cells. H&E stain, $\times 200$.

cytoplasm and round and granular nuclei, and mononuclear inflammatory cells (Fig. 2D), and infiltration of mast cells diffused in the tumor (Fig. 3D).

Immunohistochemically, cell groups was negative for pancytokeratin. The basal layer of the acini in the modified sweat gland was positive in α -SMA and vimentin while meibomian glands were positive in both cytokines (Fig. 3A, 3B, 3C).

Discussion

Although ophthalmic neoplasms are relatively uncommon in the dog, they are still the most commonly described disease of the ophthalmology and the tumor can affect any part of the eyes [9]. Tumors found in the eyelid are most commonly benign and rarely metastasize, the most common neoplasia of the eyelid is sebaceous glandular origin, including noncancerous tumors and cancerous tumors (basal cell carcinoma, squamous cell carcinoma, malignant melanoma, and sebaceous gland carcinoma) [4]. However, Ophthalmic neoplasms of pertinence to this paper are those of meibomian gland and moll gland origin

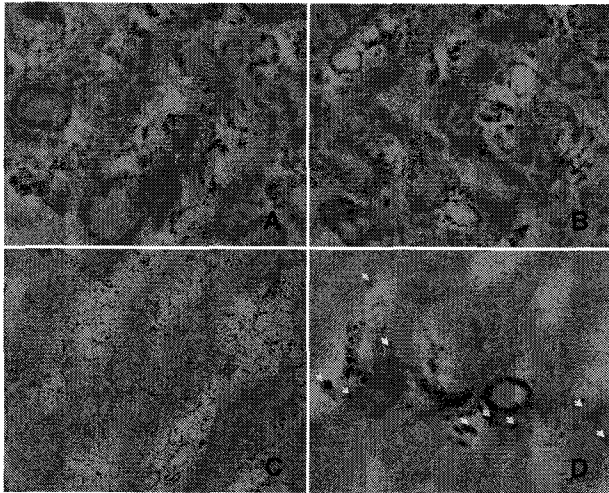


Fig. 3. Immunohistochemistry and Toluidine blue stain. A, Positive of α -SMA on the membrane tubule and acinus of modified sweat gland epithelial cells, $\times 100$. B, α -SMA positive cells on the meibomian gland epithelial cells, $\times 100$. C, Immunopositive of Vimentin in the eyelid glandular cells, $\times 50$. D, Mast cells (arrows) infiltrated between the tubular and acinar structures. TB stain, $\times 200$.

which are rare in dogs include adenomas, adenocarcinomas and mixed tumors with both connective tissue and epithelial components [12].

Neoplastic changes of the sebaceous glands of the eyelid are classified as nodular hyperplasia, epithelioma, adenoma and adenocarcinoma [7]. Sebaceous carcinoma of the eyelid is a rare malignant tumor derived from the adnexal epithelium of sebaceous glands [6]. In this case, meibomian adenocarcinoma consist of lobular structures of different sizes, having round and vesicular nuclei, well differentiated sebaceous cells of regular distribution among these lobules. The lobular structures were separated from the periphery with a well-defined margin and they were mostly of irregular shape and size which histological features resemble to those of the sebaceous tumors of the skin. Moll glands adenocarcinomas of the eyelid consist of differentiated acinar and tubular structures are lined with cubic or columnar epithelial cells having round nuclei and eosinophilic cytoplasm and considered to be of apocrine origin [13]. The changes reported in the modified sweat glands of this case were eosinophilic cytoplasm of tumor cells, decapitation luminal secretion as well having similarities with reported.

Mast cells have been implicated in pathological fibrosis in several conditions and are known to secrete a range of

some cytokines accelerate fibre production [2]. In our case, infiltration of mast cells diffused in the hyperplastic lobules of acinar and tubular structures which separated by fibrous septa, which implicated that mast cells may have pathological effect in fibre production. α -SMA is a specific marker of myofibroblasts and Vimentin expressive tumor cells invasions into actin-expression myoepithelium with focal effacement of glandular structure [14]. From this case, α -SMA and vimentin immunoreactivities not only have significant efficacy for discriminating borderline and malignant adenocarcinoma, but also elevate diagnostic sensitivity. Combined with the histopathological features of meibomian glandular and modified sweat glandular epithelial atypia and loss of polarity, these immunoreactivities assist the pathologist to more accurately assess diagnosis.

In veterinary practices, neoplastic disorders of the eyelids are rarely reported upon pathological examination and if not totally excised or removed, adenomas of the eyelid can recur and gain malignant characteristics [7]. The surgical intervention in this case was curative after the removal of the tumor mass. The histopathological examination of our case helped as arrive at the diagnosed as adenocarcinoma originating from meibomian glands and moll glands of the eyelid, and therefore infiltrating intraocular neoplasm was diagnosed as a malignant mixed adenocarcinoma. The present data provide valuable information to veterinary practitioners for the diagnosis and differentiation of neoplasms in the eyelids of dogs. Further, investigation is necessary to determine the biology of this mixed tumor.

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초록 : 개의 안검에 존재하는 내검판선 및 외검판선에서 발생한 선암종

위엔동웨이 · 구문정 · 양해걸 · 홍일화 · 기미란 · 박진규 · 이혜림 · 유성은¹ · 정규식*
 (경북대학교 수의과대학 병리학교실, ¹한국화학연구원)

본 증례는 4년령의 암컷 비글종에서 발생한 것으로 점진적인 안구돌출증을 비롯하여 왼쪽 하안구 부속기에 발생한 직경 1.4 cm의 종양을 가지고 있었다. 종양의 병리조직학적 검경에서 증생된 종양 세포들이 소엽 및 섬유성 격벽으로 구분되는 관통상의 구조를 나타내고 있었다. 잘 분화된 피지선은 다양한 크기의 소엽을 형성하고 있으며 비만세포 및 단핵 염증세포의 침윤이 관찰되었다. 관강 내에는 이러한 관성구조의 정점부위에서 탈락되어 나온 호염성 물질이 관찰되었으며 일부 관성구조는 경도의 화생을 나타내고 있었다. 조직면역염색에서 세포 집단은 α -SMA와 vimentin에 양성 반응을 나타내었다. 따라서 본 원발성 종양은 안검에서 발생한 내검판선 및 외검판선 유래의 선암종으로 진단되었으며 침윤되고 있는 안구내 종양은 악성 혼합종으로 진단되었다.