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Epithelioid leiomyosarcoma arising from the ocular region in a dog

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Abstract

A 16-year-old male mixed-breed dog presented with a mass with hemorrhage at the right conjunctiva. Five months after the initial visit, the right eye protruded and had a firm and irregular mass measuring approximately 1.00 cm in diameter with conjunctival hemorrhage. Microscopically, the mass was comprised polygonal or round tumor cells with distinct cell borders arranged in a nested and diffuse pattern. The tumor cells had round-to-oval fine hyperchromatic nuclei containing distinct multiple nucleoli and abundant eosinophilic or pale cytoplasm. Multiple giant cells were frequently observed. The mitotic index was 12.60/high power field. Extensive necrosis, hemorrhage and part of the cord-like and papillary epithelioid cells were observed in the intra-tumor tissue. Immunohistochemically, the tumor cells were positive for vimentin and α-smooth muscle actin and negative for cytokeratin, desmin and PNL2. On the other hand, the cord-like and papillary epithelioid cells were positive for vimentin, S100 and neuron-specific enolase. The tumor was diagnosed as an epithelioid leiomyosarcoma. This case considered to have occurred in the ocular region, although the ocular structure was destroyed.

Introduction

Leiomyosarcomas are malignant mesenchymal tumors of the smooth muscle that may develop in several organs, including the uterus, alimentary tract organs and skin. In humans, leiomyosarcomas are histologically classified into spindle, myxoid and epithelioid sub-types.[1] Epithelioid leiomyosarcomas (ELs) commonly occur in the uterus, heart and ovary.[1-4] The ELs are morphologically characterized by nested, corded, nodular or diffuse proliferative patterns comprising round or polygonal cells with abundant eosinophilic or pale cytoplasm.[1] The EL developing in the ocular region is extremely rare and only one case of EL occurred in the conjunctiva has been reported in human.[5]

Ocular tumors account for less than 1.00% of the total tumors in dogs, with most being malignant melanomas, iridociliary adenocarcinomas and squamous cell carcinomas.[1] Primary smooth muscle tumors occurring in the ocular region are rarely reported in dogs; however, their occurrence in the iris has been reported.[6,7]

This case is a rare case of leiomyosarcoma in the ocular region of a dog.

Case Description

A 16-year-old male mixed-breed dog was brought to an animal clinic because of a mass with hemorrhage at the right conjunctiva (Fig. 1). Five months after the initial visit, the right eye had protruded, and a firm and irregular mass was noted at the conjunctiva measured approximately 1.00 cm in diameter. A detailed examination, including hematological and serum biochemical analyses as well as radiography and ultrasonography could not be performed. However, a partially detached mass was submitted to the Department of Veterinary Pathology, Nippon Veterinary and Life Science University, Tokyo, Japan, for histopathological examination. Two months after the histological analysis, the dog died; the right ocular mass was markedly enlarged and measured approximately 4.00 cm in diameter. Necropsy was not performed at the request of the owner.

The mass was fixed in 10.00% neutral buffered formalin, processed routinely and embedded in paraffin wax. Sections were stained with Hematoxylin and Eosin (H & E) and periodic acid-Schiff (PAS). Microscopically, the mass comprised polygonal or round tumor cells with

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distinct cell borders arranged in a nested and diffuse pattern (Fig. 2A). The PAS-positive basement membrane was not observed. The tumor cells had round-to-oval fine hyperchromatic nuclei containing distinct multiple nucleoli and abundant eosinophilic or pale cytoplasm (Fig. 2B). Karyomegaly and multiple giant cells were frequently observed. The mitotic index was 12.60/high power field, and atypical mitotic figures were often detected. Extensive necrosis, hemorrhage and part of the cord-like and papillary epithelioid cells were observed in the intra-tumor tissue (Fig. 2C). No intra-vascular embolization by tumor cells was identified.

Fig. 1. Ocular conjunctival mass with hemorrhage in a 16-year-old male mixed-breed dog.

Serial sections were subjected to immunohisto-chemistry using the labelled streptavidin-biotin method and the primary antibodies for vimentin (Dako, Glostrup, Denmark), α-smooth muscle actin (SMA; Dako), cyto-keratin (CK) AE1/AE3 (Dako), CK CAM5.2 (BD Bioscience San Jose, USA), p63 (Nichirei, Tokyo, Japan), melanoma marker (PNL2; Thermo Fisher Scientific, Waltham, USA), Melan-A (Thermo Fisher Scientific), neuron-specific enolase (NSE; Dako), neurofilament (Dako), desmin (Thermo Fisher Scientific), HLA-DR (Dako), CD163 (Trans-Genic, Kumamoto, Japan), ionized calcium binding adaptor molecule-1 (Iba-1; Wako, Osaka, Japan), synaptophysin (Dako), S100 (Dako), glial fibrillary acidic protein (GFAP; Dako), c-kit carcinoembrypnic antigen (Dako), factor VIII-related antigen (Nichirei) and laminin (Abcam, Cambridge, UK). The sections were treated with 0.30% H_2O_2 (Kanto Kagaku, Tokyo, Japan) in 33.00% methanol at room temperature for 30 min to block endogenous peroxidase followed by antigen retrieval. Labelling was visualized by adding 3,3'-diaminobenzidine tetrahydrochloride (Dojindo, Kumamoto, Japan) as a chromogen and counterstain of Hematoxylin.

The primary antibodies were validated through positive reactions with appropriate normal tissue and negative reactions when normal mouse or rabbit immunoglobulin G was substituted for antibodies. Immunohistochemically, the tumor cells were positive for vimentin (Fig. 3A) and SMA (Fig. 3B), and negative for

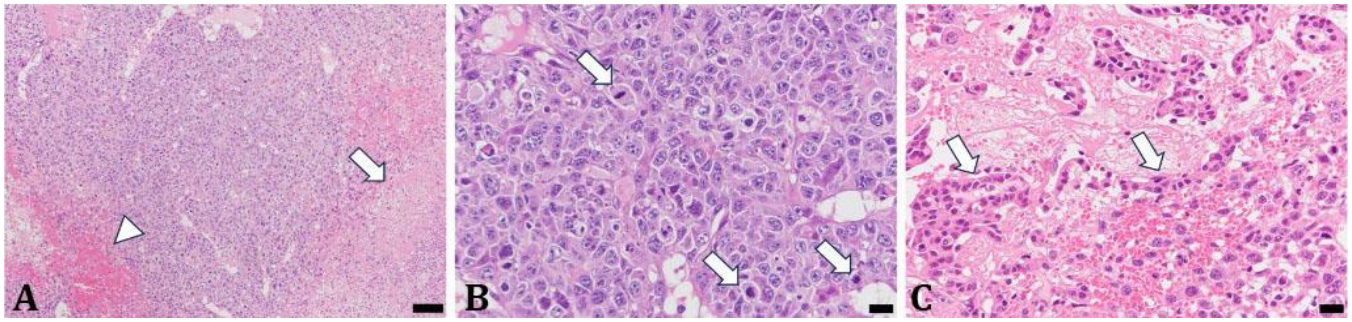

Fig. 2. Histopathological examination of ocular conjunctival mass using H & E staining. **A)** The mass was composed of polygonal or oval tumor cells arranged in diffuse pattern. Extensive necrosis (arrow) and hemorrhage (arrowhead) were observed in the intra-tumor tissue (bar = 100 μm); **B)** Polygonal or round tumor cells with distinct nucleoli and abundant eosinophilic cytoplasm. Mitoses were frequently observed which are indicated by arrows (bar = 20.00 μm); **C)** Arrows show part of the cord-like and papillary epithelioid cells in the intra-tumor tissue (bar = 20.00 μm).

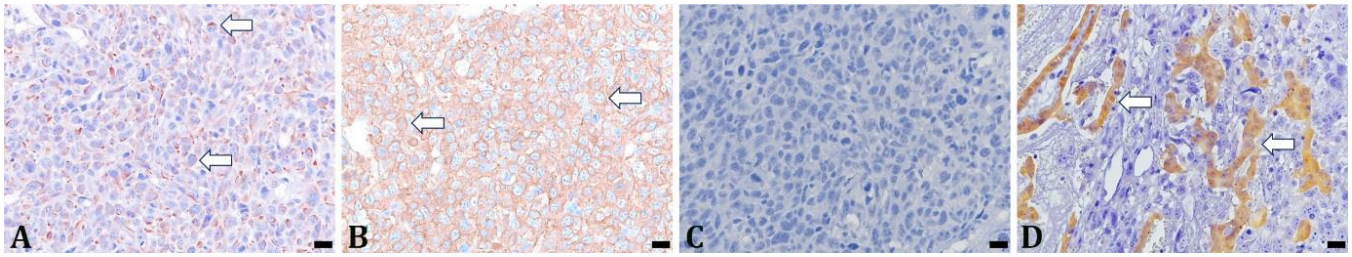

Fig. 3. Immunohistochemical (IHC) analyses of ocular conjunctival mass. **A)** The tumor cells were positive for vimentin (bar = 20.00 μm); **B)** The tumor cells were positive for a-smooth muscle actin (bar = 20.00 μm); **C)** The tumor cells were negative for Melan-A (bar = 20.00 μm); **D)** The cord-like and papillary epitheloid cells were positive for neuron-specific enolase shown by arrows (bar = 20.00 μm).

CK AE1/AE3 and CAM5.2, carcinoembryonic antigen, p63, PNL2, Melan-A (Fig. 3C), synaptophysin, S100, GFAP, NSE, neurofilament, desmin, Iba-1, HLA-DR, CD163, c-kit and factor VIII-related antigen. Also, laminin-positive basement membrane was not observed. On the other hand, the cord-like and papillary epithelioid cells were positive for vimentin, S100 and NSE (Fig. 3D). On the basis of the morphological and immunohistochemical findings, this tumor was diagnosed as an EL.

Discussion

In this case, it was necessary to differentiate EL from several tumors, including amelanotic melanomas, histiocytic sarcomas, glomus tumors and perivascular epithelioid cell tumors (PEComas). Amelanotic melanomas immunohistochemically express vimentin and melanocytic markers (PNL2 and Melan-A).[8] Histiocytic sarcomas express vimentin, CD204, Iba-1 and HLA-DR.[9] Glomus tumors, being thought to arise from modified smooth muscle cells of the glomus body, are rare in domestic animals. They consistently express vimentin and SMA, and single cells or groups of cells are surrounded by a PAS-, laminin- and collagen IV-positive basement membrane.[10] The PEComas comprise epithelioid to spindle cells being associated with blood vessel walls, and express melanocytic markers and SMA.[11] Here, the tumor was positive for vimentin and SMA expressions and negative for several markers of melanocytes and histiocytes. In addition, no PAS- and laminin-positive basement membrane was observed. Therefore, amelanotic melanomas, histiocytic sarcomas, glomus tumors and PEComas were ruled out. The ELs are diagnosed on the bases of the morphological features, such as moderate to severe atypia, mitotic index and intratumoral necrosis, as well as immunophenotype expressing muscle markers, including SMA.[1,12] In humans, ELs are often positive for CK and desmin, although the tumor was negative for both CK and desmin in this case. The significance of CK and desmin expressions in EL remains unknown.

The characteristics of EL in this case are consistent with those in humans. In normal canine eyes, vimentin and SMA-positive cells are observed in several regions, including corneal endothelium, constrictor and dilator muscles of iris, pectinate ligament, trabecular meshwork and ciliary muscles of ciliary body, lens epithelium and cortex and meninges in the optic nerves.[13] The cord-like and papillary epithelioid cells observed in this case were morphologically similar with the non-pigmented epithelium in the ciliary body, being positive for vimentin, S100 and NSE. The non-pigmented epithelia are positive for vimentin, NSE, GFAP, desmin and Melan-A.[13] On the other hand, iridociliary epithelial tumors in dogs are mainly positive for vimentin, S100 and NSE.[14] Therefore, the epithelioid cells admixed in the intra-tumor tissue may be the non-pigmented epithelium with altered immunohistochemical phenotype. Therefore, this case considered to have occurred in the ocular region, although the cell origin of this case remains unclear because the ocular structure was destroyed.

In dogs, intra-ocular leiomyoma and leiomyosarcoma have been reported, both of which originate from the iris.[6,7] Leiomyoma is localized in the iris, and leiomyosarcoma spreads to the ciliary body and cornea. However, abnormalities in the shape of the eye have not been described. On the other hand, one case of EL originating from the conjunctiva has been reported in humans, and the clinical feature of the tumor was rapid outward growth.[5] The clinical symptoms of this case were similar to those of human conjunctival EL.

In humans, ELs are considered malignant and have worse clinical manifestations, such as recurrence and metastasis, resulting in a short survival time.[3] The clinical behavior of ELs occurring in the uterus correlates with tumor necrosis, intra-vascular invasion, nuclear atypia and mitotic index (≥ 3/10 high power field).[15] However, prognostic factors for ELs have not yet been established. In this case, EL from the ocular region may have been of the high-grade type.

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Conflict of interest

The authors declare no competing interests.

References

1. Longacre TA, Lim D, Parra-Herran C. Uterine leiomyosarcoma. In: WHO classification of tumours editorial board (Eds). WHO classification of tumours editorial board. Female genital tumours. 5th ed. Lyon, France: International Agency for Research on Cancer 2020; 283-285.
2. Bouie SM, Cracchiolo B, Heller D. Epithelioid leiomyosarcoma of the ovary. Gynecol Oncol 2005; 97(2): 697-699.
3. Jellis C, Doyle J, Sutherland T, et al. Cardiac epithelioid leiomyosarcoma and the role of cardiac imaging in the differentiation of intracardiac masses. Clin Cardiol 2010; 33(6): E6-E9.
4. Kuabir A, Boudawara T, Ayadi L, et al. Epithelioid bilateral ovarian leiomyosarcoma: a study [French]. Ann Pathol 2003; 23(1): 47-49.
5. Guerriero S, Sborgia A, Giancipoli G, et al. A rare case of primitive epithelioid leiomyosarcoma of the conjunctiva. Orbit 2011; 30(3): 169-171.

6. Barron CN, Saunders LZ. Intraocular tumors in animals. II. Primary nonpigmented intraocular tumors. Cancer Res 1959; 19: 1171-1174.
7. Billson FM, Mould JRB, Lee WR. Myxoid leiomyoma of the iris in a dog. Vet Ophthalmol 2003; 6(2): 173-176.
8. Ramos-Vara JA, Miller MA. Immunohistochemical identification of canine melanocytic neoplasms with antibodies to melanocytic antigen PNL2 and tyrosinase: comparison with Melan A. Vet Pathol 2011; 48(2): 443-450.
9. Kato Y, Murakami M, Hoshino Y, et al. The class A macrophage scavenger receptor CD204 is a useful immunohistochemical marker of canine histiocytic sarcoma. J Comp Pathol 2013; 148(2-3): 188-196.
10. Burns RE, Pesavento PA, McElliott VR, et al. Glomus tumours in the skin and subcutis of three horses. Vet Dermatol 2011; 22(2): 225-231.
11. Bennett JA, Oliva E. Perivascular epithelioid cell tumors (PEComa) of the gynecologic tract. Genes Chromosomes Cancer 2021; 60(3): 168-179.
12. Howitt BE, Nucci MR. Tumors of the female genital tract. Myometrium. In: Christopher DM (Ed). Diagnostic histopathology of tumors. 5th ed. St. Louis, USA: Elsevier Saunders 2021; 831-850.
13. Labelle P, Reilly CM, Naydan DK, et al. Immunohistochemical characteristics of normal canine eyes. Vet Pathol 2012; 49(5): 860-869.
14. Dubielzig RR, Steinberg H, Garvin H, et al. Iridociliary epithelial tumors in 100 dogs and 17 cats: a morphological study. Vet Ophthalmol 1998; 1(4): 223-231.
15. Prayson RA, Goldblum JR, Hart WR. Epithelioid smooth-muscle tumors of the uterus: a clinicopathologic study of 18 patients. Am J Surg Pathol 1997; 21(4): 383-391.

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