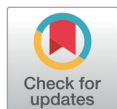


Oral leiomyosarcoma in a dog

Young Ju Kim[†], Yeseul Jeon[†], Hyoena Bae, Sun Woo Shin, ARom Cho, Jae-Eun Hyun, Tae-Sung Hwang, Il-Hwa Hong, Hee-Chun Lee, Dong-In Jung, Kyu-Woan Cho, DoHyeon Yu*

College of Veterinary Medicine, Gyeongsang National University, Jinju 52828, Korea



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[†]These authors contributed equally to this work.

*Corresponding author

DoHyeon Yu
College of Veterinary Medicine,
Gyeongsang National University, Jinju
52828, Korea
Tel: +82-55-772-2368
E-mail: yudh@gnu.ac.kr

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ORCID

Young Ju Kim
<https://orcid.org/0000-0001-6638-6952>
Yeseul Jeon
<https://orcid.org/0000-0003-3065-4729>
Hyoena Bae
<https://orcid.org/0000-0002-2888-5782>
Sun Woo Shin
<https://orcid.org/0000-0002-7978-3006>
ARom Cho
<https://orcid.org/0000-0001-9924-5056>
Jae-Eun Hyun
<https://orcid.org/0000-0002-1157-2237>
Tae-Sung Hwang
<https://orcid.org/0000-0001-6730-6061>
Il-Hwa Hong
<https://orcid.org/0000-0002-2991-2690>
Hee-Chun Lee
<https://orcid.org/0000-0001-5936-9118>
Dong-In Jung
<https://orcid.org/0000-0002-5116-6006>
Kyu-Woan Cho
<https://orcid.org/0000-0003-1301-4033>
DoHyeon Yu
<https://orcid.org/0000-0001-7645-6926>

Abstract

Leiomyosarcoma is malignant mesenchymal tumor of smooth muscle and commonly encountered in the gastrointestinal tract of dogs. However, primary canine leiomyosarcoma in oral cavity is rare due to lack of smooth muscle in the oral tissue. A 13-year-old, neutered male Poodle presented a hard and immobile mass on the left maxilla. Imprinting cytology from the mass as well as fine-needle aspirated cytology from the left scapular lymph node revealed predominant spindle cells met malignancy criteria of the tumors, including coarse chromatin, high N/C ratio, nuclear molding, macro/multi-nucleoli with cigar-shaped nucleus. Radiography of the skull showed lysis of the nasopalatine bone, and mineral radiopacity in the mass. Computed tomography showed soft tissue attenuating mass from the left incisor teeth to the left retrobulbar space with loss of nasopalatine bone and medial wall of orbit. The histopathological examination showed irregularly arranged malignant spindle-shaped cells with oval or elongated nuclei. The nucleolus is distinct and moderate cellular polymorphism is observed. Mitotic figures are occasionally observed. The tumor cells are positive to vimentin, desmin, α -smooth muscle actin when immunohistochemistry was performed, and in Masson's trichrome stain, tumor cells are stained as red. Overall, histopathologic exam and immunohistochemistry confirmed canine oral leiomyosarcoma. Because of the poor prognosis, the owner did not consent further treatment.

Keywords: leiomyosarcoma; mouth neoplasms; immunohistochemistry; vimentin; desmin

INTRODUCTION

Canine oral tumor is relatively common accounting for 6% of all tumors in dogs. The most common oral tumors in dogs include malignant melanoma, squamous cell carcinoma, fibrosarcomas [1–3]. Leiomyosarcoma is a malignant mesenchymal tumor originated from smooth muscle [4]. Leiomyosarcoma constitutes 20 to 30 per cent of all intestinal neoplasms in dogs [5], however, oral leiomyosarcoma is scarce owing to paucity of smooth muscle structures in this location [6]. Therefore, no specific reference to their diagnosis, management and prognosis has been reported up to date [7]. Herein, we report maxillary leiomyosarcoma in a dog confirmed by immunohistochemistry.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

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Ethics Approval

Not applicable.

CASE REPORT

A 13-year-old, neutered male Poodle was administered to veterinary medical teaching hospital in Gyeongsang National University for left maxillary mass. Initially, a small-sized mass (<1 cm) was found on the upper body of the maxilla, and it enlarged rapidly for the last 4 weeks. It was not responsive to antibiotics prescribed from the local veterinary clinic, and recently accompanied by dysphagia, hyporexia, and hemorrhage. Oral examination revealed a 4.8 cm × 2.5 cm-sized hard and immobile mass was observed on the left maxilla (Fig. 1A). Left prescapular lymph node was also enlarged, but no abnormalities in core temperature, pulse rate, and respiratory rate were found. A complete blood count revealed normocytic normochromic regenerative anemia (hematocrit [HCT], 33.6%; reference range, 37.3%–61.7%; reticulocyte count, $117.6 \times 10^3/\mu\text{L}$), leukocytosis ($18.07 \times 10^3/\mu\text{L}$; reference range, $5.05\text{--}16.76 \times 10^3/\mu\text{L}$), and thrombocytosis ($651 \times 10^3/\mu\text{L}$; reference range, $148\text{--}484 \times 10^3/\mu\text{L}$). Serum biochemistry analysis revealed hyperglobulinemia (4.8 mg/dL; reference range, 2.5–4.5 mg/dL) (Table 1). Thromboelastography (TEG) to determine the risk of hypercoagulability of the tumor revealed high MA, short K evaluated as hypercoagulable state. Cytological evaluation of the maxillary mass showed predominant spindle cells met malignancy criteria of tumor cells, including coarse chromatin, high N/C ratio, nuclear molding, macro/multi-nucleoli with cigar-shaped nucleus (Fig. 1B). Cytological evaluation of the enlarged left scapular lymph node by fine needle aspiration also revealed metastasis-associated malignant cells. Radiography of the skull showed lysis of the nasopalatine bone, and mineral radiopacity in the mass (Fig. 2A). Computed tomography showed soft tissue attenuating mass from the left incisor teeth to the left retrobulbar space with loss of nasal bone, palatine bone and orbital medial wall (Fig. 2B). The histopathological examination showed the irregularly arranged spindle-shaped cells, and oval or elongated nuclei of the tumor cells. The nucleolus is distinct and moderate cellular polymorphism is observed. Mitotic figures are occasionally observed (Fig. 3). The tumor cells are positive to vimentin, desmin, α -smooth muscle actin when immunohistochemistry was performed using anti-vimentin, anti-desmin, anti-alpha smooth muscle actin (α -SMA) (Santa Cruz Biotechnology, Dallas, TX, USA) antibodies. In Masson's trichrome stain, tumor cells are stained as red (Fig. 4). Overall, histopathologic exam and immunohistochemistry

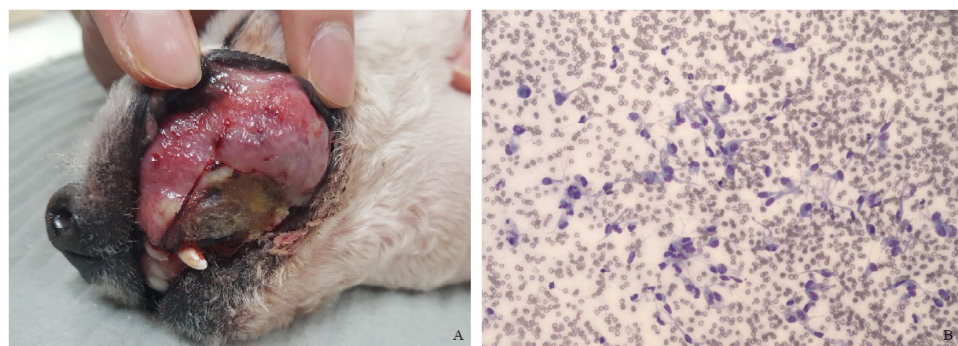
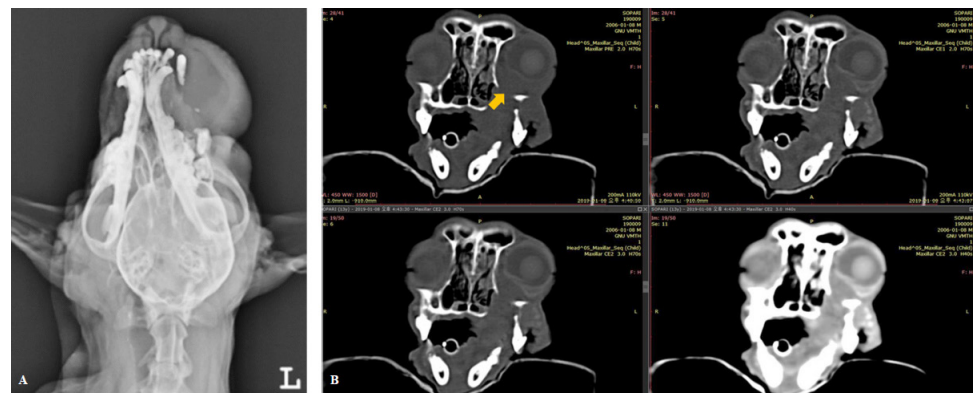
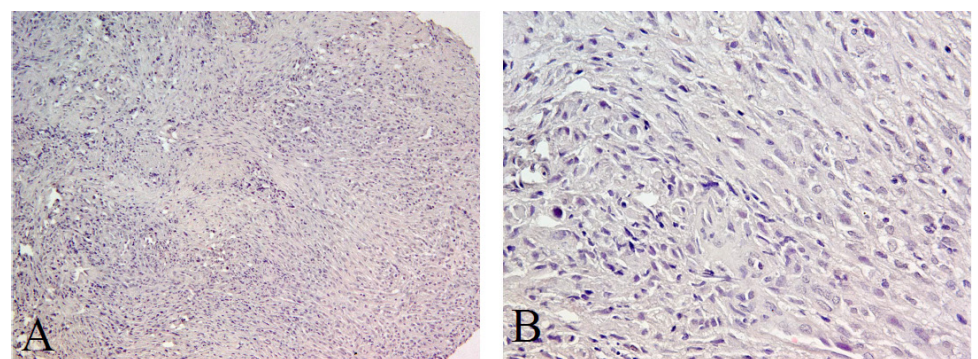


Fig. 1. Macroscopic and microscopic examination of the oral leiomyosarcoma. (A) A hard and immobile mass located on the left maxilla of the oral leiomyosarcoma. (B) Cytologic examination of the mass showing predominant malignant spindle-shaped cells satisfying malignancy criteria of tumor cells.

Table 1. Clinicopathologic analysis in a dog with leiomyosarcoma

Complete blood count	Results	Reference intervals	Serum biochemistry	Results	Reference intervals
Red blood cells	5.14	5.65–8.81 ($\times 10^9/L$)	Glucose	103	74–143 (mg/dL)
Hematocrit	33.6	37.3–61.7 (%)	Creatinine	0.5	0.5–1.8 (mg/dL)
Hemoglobin	11	13.1–20.5 (g/dL)	Urea nitrogen	10	7–27 (mg/dL)
Mean red cell volume	65.4	61.6–73.5 (fL)	Phosphorus	4.9	2.5–6.8 (mg/dL)
Mean cell hemoglobin concentration	32.7	32–37.9 (g/dL)	Calcium	10	7.9–12 (mg/dL)
White blood cells	18.07	5.05–16.76 ($\times 10^9/L$)	Total protein	7.5	5.2–8.2 (mg/dL)
Neutrophils	12.67	2.95–11.64 ($\times 10^9/L$)	Albumin	2.8	2.3–4 (g/dL)
Lymphocytes	2.16	1.05–5.10 ($\times 10^9/L$)	Globulin	4.8	2.5–4.5 (g/dL)
Monocytes	2.73	0.16–1.15 ($\times 10^9/L$)	Alanine aminotransferase	26	10–125 (U/L)
Eosinophils	0.49	0.06–1.23 ($\times 10^9/L$)	Alkaline phosphatase	57	23–212 (U/L)
Basophils	0.02	0.00–0.10 ($\times 10^9/L$)	Gamma-glutamyl transferase	3	0–11 (U/L)
Platelet count	393	148–484 ($\times 10^9/L$)	Total bilirubin	0.1	0–0.9 (mg/dL)
			Cholesterol	139	110–320 (mg/dL)
			Triglyceride	83	10–100 (mg/dL)
			Amylase	812	500–1,500 (U/L)
			Lipase	544	200–1,800 (U/L)

**Fig. 2.** Diagnostic imaging analysis of the dog with oral leiomyosarcoma. (A) Radiography of the skull showed bone lysis, and mineral opacity. (B) Computed tomography showed soft tissue attenuating mass from the left incisor teeth to the left retrobulbar space with loss of nasal bone, palatine bone and orbital medial wall (arrow).**Fig. 3.** Histopathologic examination of the mass. (A) the spindle-shaped cells are irregularly arranged. (B) The nuclei of the tumor cells are oval or elongated. The nucleolus of the tumor cells is distinct, and cellular polymorphism is moderated. Mitotic figures are occasionally seen. H&E, Original magnifications: 100 \times (A), 400 \times (B).

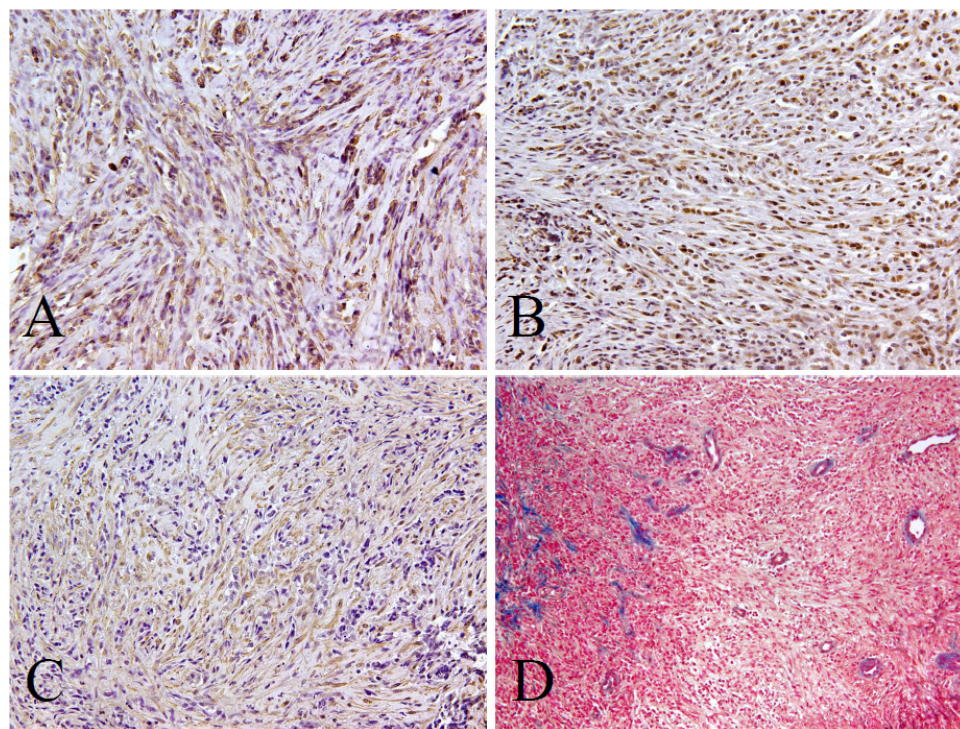


Fig. 4. Immunohistochemistry and Masson's trichrome stain of the mass. (A) The tumor cells are positive to vimentin, (B) desmin, (C) α -smooth muscle actin. (D) In Masson's trichrome stain, tumor cells are stained as red. A few Fibroblasts and some collagen in the vessels or connective tissue are stained as blue. Original magnifications: 100 \times (D), 200 \times (A, B, C).

confirmed canine oral leiomyosarcoma. However, owner did not consent surgical resection. Esophageal tubing for palliative therapy was applied and follow up was lost.

DISCUSSION

Leiomyosarcoma is malignant mesenchymal tumor of smooth muscle. The most common site of the leiomyosarcoma is gastrointestinal tract, such as stomach, esophagus, small intestine, and colorectum in dogs [1, 8–11]. Oral leiomyosarcoma is rare in dogs due to lack of smooth muscle tissue in the oral cavity. Several reports suggested that the major sources of smooth muscle in the oral cavity are the walls of blood vessels or displaced embryonal tissue, the vascular system of bone or accessory salivary glands [6, 12]. Since it is not commonly encountered in veterinary clinic, leiomyosarcoma should be confirmed by histopathology and immunohistochemistry. The cells are typically composed of long, plump spindle cells, which have cytoplasm with oval blunt-ended nuclei, perinuclear vacuoles, and frequent nuclear chromatin crossbars, but collagenous stroma is little. Leiomyosarcomas are positive for vimentin, α -smooth muscle actin as well as desmin in the immunohistochemistry [13, 14]. The present case present oral mass on the left maxilla, and leiomyosarcoma was confirmed by immunohistochemistry. Sarcomas can be the top of the differential list for cigar-like nuclear morphology and spindle cells met malignant criteria of the tumor cells. In case of oral sarcomas, leiomyosarcoma can be considered if cytological analysis are consistent with smooth muscle-origina-

ed cells.

In human, the prognosis of leiomyosarcoma is poor, with a high percentage of recurrence or metastasis. The most common sites of metastasis include the lungs, bone, brain and the lymph node [15]. The most effective treatment of the leiomyosarcoma is radical surgical excision with adequate margins [10, 16]. For inoperable tumors or those in difficult sites such as the mandibular condyle or maxillary sinus, radiotherapy can be used in addition to surgery [17]. Chemotherapy appeared to be ineffective unless it was used as a palliative measure in patients with widespread metastatic disease [18]. Kapatkin et al. reported that the prognosis in dogs with leiomyosarcoma of the spleen, stomach, small intestine, and especially the cecum is good if surgery is performed [5]. Though it has not been sufficiently studied in dogs, the site of the leiomyosarcoma is more important for prognosis when compared to human study: those arising in a superficial cutaneous localization have the best prognosis [15] whereas bony involvement is a potential negative prognostic indicator in human [19]. In the present case, there was an extensive soft tissue mass from the left incisor teeth to the left retrobulbar space with bone invasion, thus complete excision with surgery was impossible. Unfortunately, proper treatment options were not applied, but the prognosis might not be good considering given the size and the location of the lesion.

REFERENCES

1. Liptak J. Cancer of the gastrointestinal tract. In: Withrow and Macewen's small animal clinical oncology. 6th ed. St. Louis: Elsevier; 2007. p. 462.
2. Vos JH, van der Gaag I. Canine and feline oral-pharyngeal tumours. *Zentralbl Veterinarmed A* 1987;34:420-427.
3. Todoroff RJ, Brodey RS. Oral and pharyngeal neoplasia in the dog: a retrospective survey of 361 cases. *J Am Vet Med Assoc* 1979;175:567-571.
4. Amarapala H, Tilakaratne WM. Leiomyosarcoma of the oral cavity: report of seven cases and review of literature. *Oral Oncology Extra* 2006;42:14-17.
5. Kapatkin AS, Mullen HS, Matthiesen DT, Patnaik AK. Leiomyosarcoma in dogs: 44 cases (1983–1988). *J Am Vet Med Assoc* 1992;201:1077-1079.
6. Takagi M, Ishikawa G. An autopsy case of leiomyosarcoma of the maxilla. *J Oral Pathol Med* 1972;1:125-132.
7. Boy SC, Van Heerden WFP, Steenkamp G. Diagnosis and treatment of primary intraoral leiomyosarcomas in four dogs. *Vet Rec* 2005;156:510-513.
8. Frost D, Lasota J, Miettinen M. Gastrointestinal stromal tumors and leiomyomas in the dog: a histopathologic, immunohistochemical, and molecular genetic study of 50 cases. *Vet Pathol* 2003;40:42-54.
9. LaRock RG, Ginn PE. Immunohistochemical staining characteristics of canine gastrointestinal stromal tumors. *Vet Pathol* 1997;34:303-311.
10. Penninck DG. Characterization of gastrointestinal tumors. *Vet Clin North Am Small Anim Pract* 1998;28:777-797.

11. Lo Muzio L, Favia G, Farronato G, Piattelli A, Maiorano E. Primary gingival leiomyosarcoma: a clinicopathological study of 1 case with prolonged survival. *J Clin Periodontol* 2002;29:182-187.
12. Izumi K, Maeda T, Cheng J, Saku T. Primary leiomyosarcoma of the maxilla with regional lymph node metastasis. Report of a case and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol* 1995;80:310-319.
13. Gross TL, Ihrke PJ, Walder EJ, Affolter VK. Smooth muscle and skeletal muscle tumors. In: Gross TL, Ihrke PJ, Walder EJ, Affolter VK (eds.). *Skin diseases of the dog and cat: clinical and histopathologic diagnosis*. 2nd ed. Ames: Blackwell; 2008. p. 778-785.
14. Andreasen CB, Mahaffey EA. Immunohistochemical demonstration of desmin in canine smooth muscle tumors. *Vet Pathol* 1987;24:211-215.
15. Pinheiro JJV, Alves SM, Okuda E, Jorge WA, Jaeger RG, de Araújo NS. Primary leiomyosarcoma of the mandible. A case report. *Med Oral Patol Oral Cir Bucal* 2007;12:56-59.
16. Goldschmidt PR, Goldschmidt JD, Lieblich SE, Eisenberg E. Leiomyosarcoma presenting as a mandibular gingival swelling: a case report. *J Clin Periodontol* 1999;70:84-89.
17. Schenberg ME, Slootweg PJ, Koole R. Leiomyosarcomas of the oral cavity. Report of four cases and review of the literature. *J Craniomaxillofac Surg* 1993;21:342-347.
18. Fields JP, Helwig EB. Leiomyosarcoma of the skin and subcutaneous tissue. *Cancer* 1981;47:156-169.
19. Recine F, Bongiovanni A, Casadei R, Pieri F, Riva N, De Vita A, Mercatali L, Liverani C, Spadazzi C, Miserocchi G, Fausti V, Amadori D, Ibrahim T. Primary leiomyosarcoma of the bone: a case report and a review of the literature. *Medicine* 2017;96:e8545.