NOTE *Pathology*

Oral Leiomyosarcoma in a Woodchuck (*Marmota monax*)

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ABSTRACT. We report the case of a 4-year-old female woodchuck (*Marmota monax*) which presented with a white, firm and discrete mass in the hard palate. The mass extended into the oral cavity but it was well separated from the surrounding tissues. Histology of the tumor showed a malignant mesenchymal tumor with pleomorphic spindle cells varying in degrees of differentiation and density. The neoplastic cells had moderate amounts of granular or fibrillar eosinophilic cytoplasm with indistinct cell margins. Nuclei were oval to elongated and frequently blunt-ended with vesicular chromatin. Immunohistochemical study showed that the neoplastic cells expressed vimentin and alpha-smooth muscle actin but did not express desmin, pan-cytokeratin, and S-100. Therefore, histology and immunohistochemistry revealed that the tumor was oral leiomyosarcoma. Oral cavity is an extremely rare site for leiomyosarcoma and the present case is the first report of spontaneous oral leiomyosarcoma in animals.

KEY WORDS: leiomyosarcoma, oral neoplasm, woodchuck.

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Leiomyosaroma is a slow-growing, malignant tumor of smooth muscle and constitutes only 10% of the total smooth muscle tumors [5]. It has been reported in the kidney, ovary, and skeletal muscle [5]. Leiomyosarcoma is the second most common intestinal tumor in dogs [2, 3], but in a recent retrospective study of 44 cases, the spleen has been reported as the most common site [8]. In animals and humans, leiomyosarcoma of the oral cavity is extremely rare. This report first describes the histopathological and immunohistochemical features of a primary hard palate leiomyosarcoma in a woodchuck.

A 4-year-old female woodchuck (*Marmota monax*) housed at the Shinwon Science, Inc. (Seoul, Korea) for the efficacy study of an experimental anti-HBV substance was presented with an acute onset of hematemesis, nasal discharge, and dyspnea with pulmonary murmur. It was a member of breeding colony and had no significant prior health problems except reduction in appetite. Because the animal did not respond to treatments and its conditions got worse, it was euthanatized. At necropsy, a white, firm and discrete mass, 40 × 70 × 15 mm in diameter, was observed in the hard palate (Fig. 1). The tumor mass extended into oral cavity but well separated from the surrounding tissues. The cut-surface of the tumor was solid and colored white to pink. No abnormal gross lesions were found in the other organs except that a right mandibular lymph node was enlarged.

The tumor mass was fixed in 10% neutral phosphated-buffered formalin solution. The tissue was trimmed, dehydrated in a graded series of ethanol, and embedded in paraffin. Sections for microscopic examination were made at a thickness of 4 μm and stained with hematoxylin and eosin (H&E). For immunohistochemical studies, additional paraffin sections were examined by the avidin-biotin-peroxidase complex (ABC) with appropriate uses of positive and negative controls throughout. The antibodies were used as follows: anti-desmine, anti-alpha-smooth muscle cell actin, anti-vimentin, anti-S-100, and anti-pan-cytokeratin (DAKO, Carpinteria, CA, U.S.A). Dilutions were made 1:150, 1:150, 1:100, 1:500, and 1:500, respectively.

Histopathologically, the tumor mass consisted of interlacing fascicles of spindled cells varying in degrees of differentiation and density. The tumor cells had moderate amounts of granular or fibrillar eosinophilic cytoplasm with indistinct cell margins. Tumor cell nuclei were generally oval to elongated and somewhat vesicular. Various sizes of prominent nucleoli were also present. In more poorly differentiated areas of the tumor, the cells lost spindle shape and became round. Nuclei in these cells were pleomorphic and rather round. Nucleoli were prominent and had coarsely clumped chromatin. Mitotic figures were numerous in these areas (Fig. 2). In addition, tumor mass was necrotic and the area of necrosis was infiltrated with neutrophils.

The enlarged right mandibular lymph node was filled with neoplastic cells. Metastatic tumor nodule occupied 70 to 80% of the lymph node. Tumor cells in the lymph node had the same organization of interlacing fascicles of spindled cells, but tumor cells with atypical nuclei and significant variations in sizes were increased in the lymph node (Fig. 3).

Neoplastic cells stained red with Masson's trichrome stain. Immunohistochemistry of the tumor mass and the lymph node revealed the positive cytoplasmic staining of neoplastic cells for alpha-smooth muscle actin (Fig. 4) and vimentin, but cells were negative for desmin, pan-cytokeratin, and S-100. Histological and immunohistochemical findings supported a diagnosis of an oral leiomyosarcoma.

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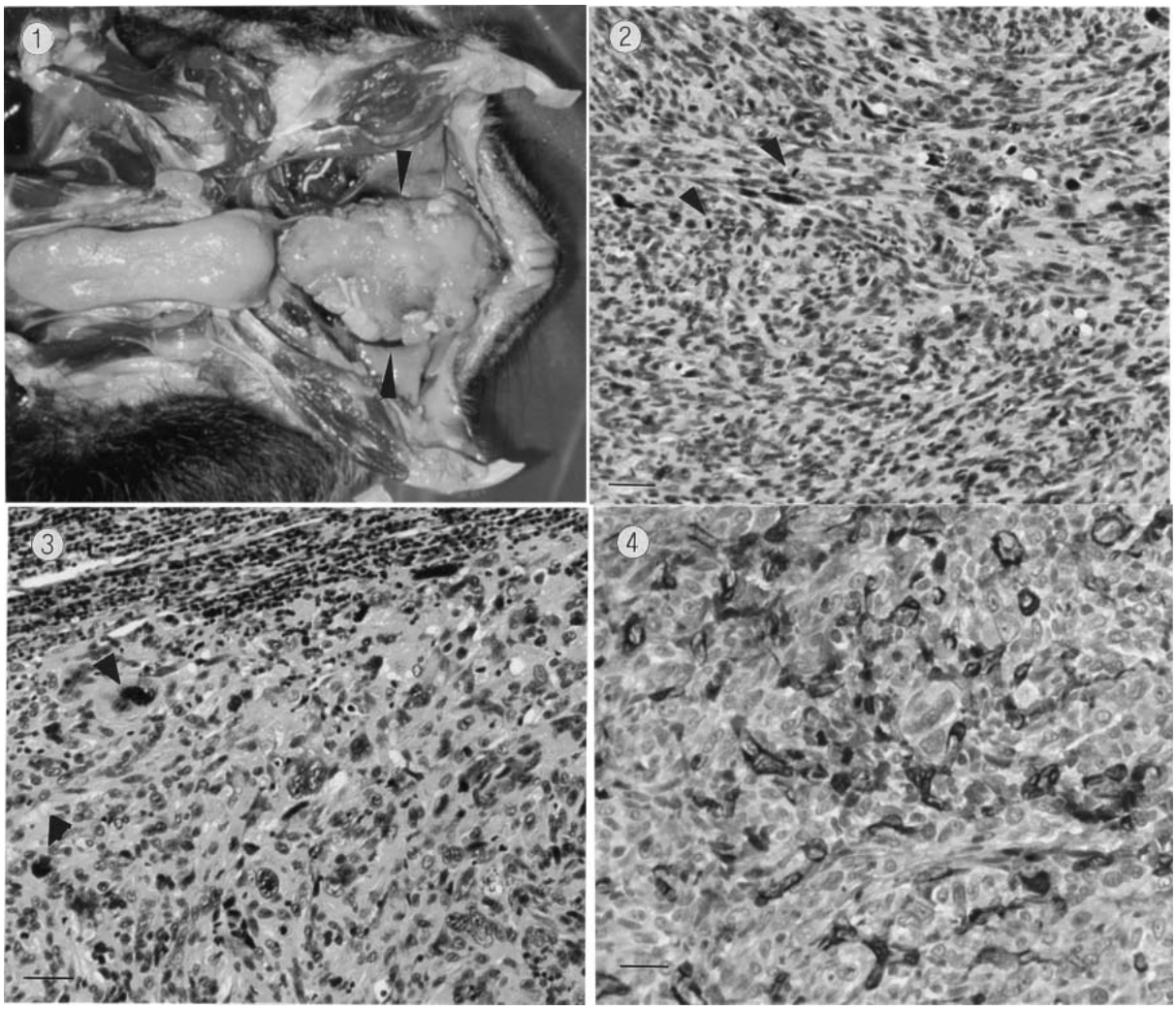

Fig. 1. A white, firm discrete mass extended into the oral cavity was observed in the hard palate.
Fig. 2. Pleomorphic spindle-shaped cells with small to large nuclei showing intersecting fascicular architecture. Many mitotic figures (arrow heads) observed. H&E. Bar = 55 μm.
Fig. 3. Nuclear atypia was prominent in the tumor metastasized into the lymph node. Note the atypical mitotic figures (arrow heads). Bar=20 μm.
Fig. 4. Alpha-smooth muscle cell actin immunoreactivity was observed in the majority of tumor cells. Avidin-biotin peroxidase complex method. Mayer's hematoxylin countertstain. Bar=55 μm.

Leiomyosarcoma is a malignant mesenchymal tumor that is relatively common in the uterus and gastrointestinal tract in animals [2, 3]. The incidence of oral leiomyosarcoma is very rare and there has been no reported case in animals. The incidence of oral leiomyosarcoma in human is also very rare and it has been only 70 cases reported [6, 12]. The rare incidence is attributed to the scarcity of smooth muscle in the location. Approximately, 50% of oral leiomyosarcomas in human comes from maxilla and mandible [6, 10]. Other reported intraoral locations include cheek, tongue, hard and soft palate, lips, gingival and floor of mouth [12]. The origin of oral leiomyosarcoma is suggested to be from the circumvallate papilla of the tongue, from undifferentiated mesenchyme, and from smooth muscle in vessel walls [9].

Oral leiomyosarcoma is very aggressive tumor with high incidences of recurrence and metastasis. Survival rate from the tumor is very low. Unlike leiomyosarcomas in soft tissue elsewhere, occasional metastasis to regional lymph nodes has been reported in human oral leiomyosarcoma [6, 10]. We could also find metastasis to regional lymph nodes in the present case. The proportion of malignancies among smooth muscle tumors of oral cavity is high [12]. Histologic features such as cellular atypia, a number of mitosis, and varying degree of cell density were observed and they represented the degree of malignancy in the present case.

A definitive diagnosis of leiomyosarcoma is generally

established on the basis of light microscopic and immunohistological examinations. The differential diagnosis must exclude the possibility of fibrosarcoma, rhabdomyosarcoma, malignant schwannoma, and non-pigmented melanoma. Demonstration of myofibrils and centrally located cigar-shaped nuclei is known as helpful histological feature [5]. In this case, histological characteristics of tumor cells with fascicular growth pattern and immunoreactivity for alpha-smooth muscle actin (Fig. 4) and vimentin were consistent with previous descriptions of leiomyosarcoma. Negative immunoreactivity for desmin could raise an objection against the origin of tumor cells from smooth muscle. However, a few cases of leiomyosarcoma with absent or weak desmin expression have been reported in canine and feline leiomyosarcomas [1, 4, 7]. In addition, desmin-negative leiomyosarcoma has been described in man [11]. Occasionally, malignant schwannoma and non-pigmented melanoma with spindle-shaped may mimic leiomyosarcoma. Negative staining for S-100 protein and cytokeratins with positive staining for myogenic markers indicated a mesenchymal tumor with smooth muscle differentiation.

Taken together, we first report a case of oral leiomyosarcoma in a woodchuck.

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