

Extraskkeletal Osteosarcoma of the Mandibular Salivary Gland in a Dog

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Abstract. A 14-year-old spayed female shepherd/collie crossbred dog had a 6 × 4-cm mass excised from below the right ear. The partially encapsulated, neoplastic mass had a necrotic core and was embedded in the mandibular salivary gland. Histologically, the mass was composed of numerous multinucleate giant cells and large, oval, pleomorphic cells that produced osteoid. Neoplastic cells were immunoreactive for vimentin and actin but not for keratin, desmin, or S-100 protein. At postmortem examination 1 month later, an 11-cm spherical mass had recurred at the surgical site, and there were metastatic nodules in the lungs, ipsilateral mandibular lymph nodes, and kidney. The tumor was diagnosed as an osteosarcoma of the mandibular salivary gland with pulmonary, lymphatic, and renal metastasis. In addition, a 17-year survey of canine salivary-gland neoplasms revealed that most were adenocarcinomas or carcinomas.

Key words: Dogs; immunohistochemistry; osteosarcoma; salivary gland neoplasms.

Salivary-gland neoplasms and extraskkeletal osteosarcomas are both rare in dogs.^{3,9,10} Salivary neoplasms make up 0.09% of all canine surgical biopsies in one report.³ Extraskkeletal osteosarcomas have been reported to make up approximately 1% of all canine osteosarcomas.⁹ Numerous types of salivary-gland tumors have been reported, as have various classification schemes.^{3,5,8,10} One recent review classified tumors as adenocarcinoma, carcinoma, squamous-cell carcinoma, mixed, primary fibrosarcoma, mast-cell tumor, adenoma, and unspecified.³ Other studies have included mucoepidermoid, acinic cell, malignant mixed, true malignant mixed, malignant melanoma, secondary fibrosarcoma, and secondary lymphosarcoma.^{5,8,10,13} Bone has been reported in mixed tumors (pleomorphic adenomas), malignant mixed tumors (carcinoma in pleomorphic adenomas), and true malignant mixed tumors (carcinosarcomas).^{2,4,6,13} The vast majority of salivary-gland tumors are adenocarcinomas and carcinomas according to our study and others.^{3,10} Extraskkeletal osteosarcomas have been reported as primary tumors in a variety of soft tissues, but not in salivary glands.⁹ In this paper, we present histopathologic and immunohistochemical evidence of a malignant mandibular salivary-gland tumor that consisted only of an osteosarcoma, and we briefly summarize 43 cases of additional canine salivary-gland tumors.

An excisional biopsy was submitted in 10% neutral buffered formalin to the Iowa State University College of Veterinary Medicine, Department of Veterinary Pathology, from a 14-year-old spayed female shepherd/collie crossbred dog. The rapidly growing mass had been known to be present for approximately 2 weeks before being surgically removed. It was described as hard, fixed, encapsulated, vascular, and originating ventral to the right ear and extending under the mandible. Grossly, the surface of the oval mass was light gray, rough, and fibrous, measuring 6 cm long and 4 cm in diameter. A tan, lobulated, glandular structure (mandibular salivary gland) was embedded in the neoplastic tissue. On cut section, the mass had a 5–10 mm layer of white, gray, firm, and occasionally gritty peripheral rim surrounding a necrotic friable core (Fig. 1). Samples of the mass were embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin (HE), Masson's trichrome, periodic acid–Schiff, and Giemsa stain. Further samples were exam-

ined after decalcification in 25% formic acid solution for 3 days.

Histologically, the expansile mass had a necrotic center and was incompletely surrounded by a thick fibrous capsule. The mandibular salivary gland had been largely replaced, leaving only a small area of normal mucous and serous glands. A haphazard arrangement of large oval to spindle-shaped and round cells produced varying amounts of eosinophilic osteoid matrix and comprised the bulk of the mass (Fig. 2). Some of the osteoid was mineralized, and neoplastic cells were located within osteoid lacunae. Cytoplasm varied from scanty, pale, and eosinophilic to abundant, dark, eosinophilic, and granular. The nuclei were hyperchromatic and had one to three large, prominent nucleoli. The mitotic index was 46/10 400× fields, and bizarre mitotic figures were common. Large numbers of multinucleate giant cells with darkly eosinophilic cytoplasm were disseminated throughout the section. They contained variably shaped nuclei numbering from two to more than twenty. Often these cells lined osteoid. Within the capsule, clumps of neoplastic cells were surrounded by lymphocytes and fewer plasma cells near the surgical margins. Neoplastic cells were also found within capsular vessels. Several areas contained hemorrhage, macrophages filled with hemosiderin, and neutrophils. The center of the mass was filled with cellular debris, fibrin, necrotic bone, and hemorrhage. Periodic acid–Schiff stains highlighted normal mucous glands, but did not stain the neoplastic cells. Masson's trichrome and Geimsa stain contributed little additional information.

Representative 3-μm sections were stained by standard streptavidin-biotin immunoperoxidase methods with the following primary antibodies: monoclonal mouse antivimentin (Dako Corp.), rabbit polyclonal antikeratin wide-spectrum screening (Dako), monoclonal mouse anti-human muscle actin (Dako), mouse monoclonal anti-human desmin (Zymed Laboratories, Inc.), and rabbit anti-S-100 protein, (Zymed). Negative control sections of the tumor lacked primary antibody, and positive control tissue sections were included for each antibody. Most cells were immunoreactive for vimentin, including those neoplastic cells adjacent to osteoid. A large number of cells also were immunoreactive for actin. The neoplastic cells did not stain for keratin, desmin, and S-

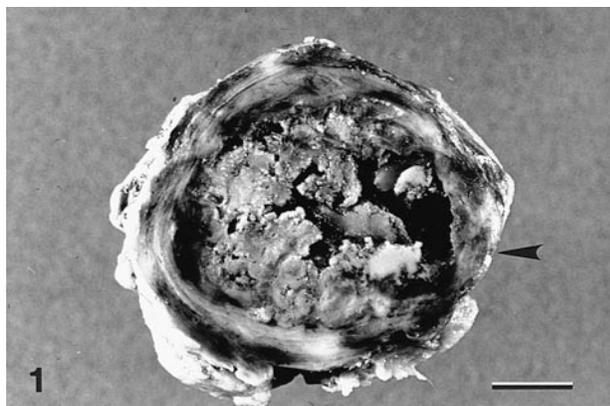


Fig. 1. Mandibular salivary gland, sagittal section; dog. Osteosarcoma has replaced most of the glandular tissue (arrowhead) and has a large necrotic core. Bar = 1 cm.

100. A small focus of normal glandular epithelium stained for keratin.

After the biopsy diagnosis of osteosarcoma, the dog was re-examined and no clinical signs of a skeletal osteosarcoma were found. Skull radiographs showed no bone involvement at the surgical site or elsewhere. Thoracic radiographs revealed several small radiodense areas within the lungs that were suggestive of metastatic disease.

Approximately 1 month after surgery, the mass had recurred and the owners requested euthanasia. On postmortem examination, the dog had an 11-cm spherical mass centered slightly ventral and cranial to the right horizontal ear canal. On cut section, the mass contained a large necrotic core that was red to black and friable. The outer 1–3 cm was white to gray and firm. The invasive mass replaced all normal tissue in the area and extended deeply to within 5 mm of the mandible. The ipsilateral mandibular lymph nodes were slightly enlarged and had multiple 2–3 mm white areas on cut section. All lung lobes contained multifocal 5–15 mm raised, white, spherical masses. On cut section the masses were dark red and distributed throughout the lung parenchyma. One kidney contained two 1–2-cm white to gray cortical masses. Microscopically, the morphologic and staining characteristics for the masses were similar to the initial tumor. HE-stained sections confirmed that there was metastasis to the lung, kidney, and ipsilateral mandibular lymph nodes. Lung and renal sections both contained areas of osteoid. Based on these findings, an osteosarcoma of the mandibular salivary gland with pulmonary, renal, and lymphatic metastasis was diagnosed.

In our search for previous salivary gland osteosarcomas, we reviewed 35,609 canine submissions to our department between 1980 and 1997, of which 140 (0.4%) included salivary gland tissue. Forty-three (31%) of the 140 salivary gland submissions, or 0.1% of the total submissions, were neoplastic. The majority of these neoplasms were adenocarcinomas and carcinomas. The remaining were malignant mixed tumors, metastatic lymphosarcomas, and an osteosarcoma, the present case. There were no benign neoplasms (Table 1). These findings are similar to other published reports.^{3,10}

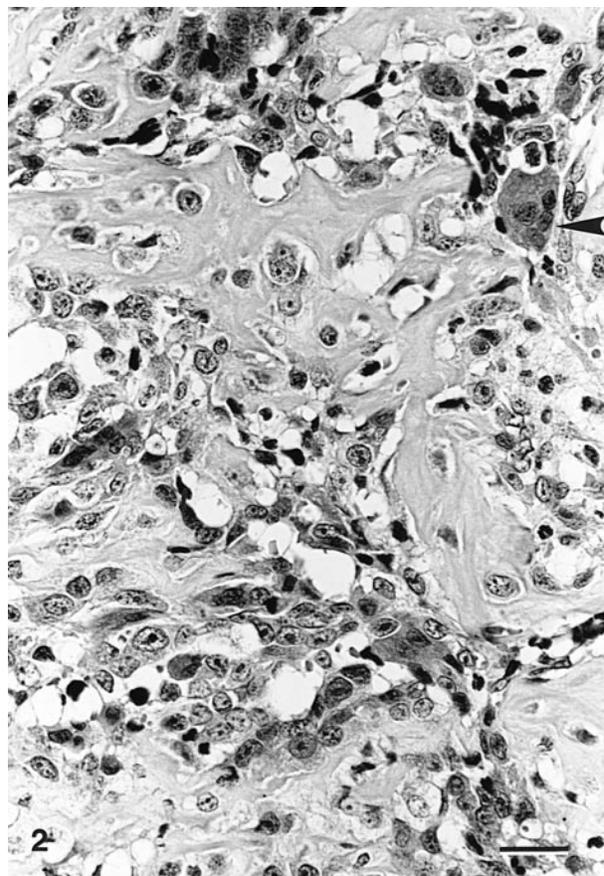


Fig. 2. Mandibular salivary gland; dog. Irregularly arranged round to oval neoplastic cells have produced and are enclosed in osteoid matrix. A multinucleated giant cell is adjacent to the osteoid matrix (arrowhead). HE. Bar = 20 μm.

The mass in this report was termed an osteosarcoma and not a malignant mixed tumor based on its morphology and staining characteristics, as well as the lack of morphology and immunohistochemical evidence of any neoplastic epithelial cells in multiple sections. Because we found no evidence of a primary skeletal tumor, carcinosarcoma, mesenchymoma, differentiating teratoma, or metaplastic change, the neoplasm fit the criteria of extraskeletal osteosarcoma.⁹

Table 1. Morphologic diagnosis of 43 canine salivary-gland neoplasms submitted to Iowa State University, Department of Veterinary Pathology, between 1980 and 1997.

Morphologic Diagnosis	No. of	
	Cases	Percentage
Adenocarcinoma	23	(53%)
Carcinoma	15	(35%)
Malignant mixed tumor*	2	(5%)
Secondary neoplasia (lymphosarcoma)	2	(5%)
Osteosarcoma†	1	(2%)

* Carcinoma in pleomorphic adenoma.

† The present case.

The aggressive local behavior and early metastasis were also consistent with osteosarcoma.

We were unable to find any previously reported primary salivary-gland osteosarcomas in domestic animals. Primary osteosarcomas have been reported in human salivary glands.¹² When immunohistochemistry was performed on three of these tumors, all three were immunoreactive to vimentin and nonreactive to keratin, S-100, actin, and desmin.¹² The few canine mixed malignant salivary-gland tumors in veterinary literature fit the definition of carcinoma in pleomorphic adenomas or were not fully described.^{3,5,10,13} Salivary-gland tumors in a cat and a cow with both adenocarcinomatous and sarcomatous components have been described; the latter contained trabeculae of bone.¹³ In humans, carcinosarcomas that have an osteosarcoma component are rare.^{2,4} A variety of other primary human salivary-gland sarcomas have also been reported.¹

The origin of osteosarcomas in salivary glands is unknown, but it may be an anaplastic myoepithelial cell or an undifferentiated pluripotential cell.¹ Salivary glands, like mammary glands, originate from ectoderm and have a similar cellular makeup.⁷ Primary extraskeletal canine mammary osteosarcomas are well documented and reported to be immunoreactive for vimentin (4/4), desmin (3/4), and cytokeratin (1/4), but not for neurofilament (0/4).⁷ Other canine extraskeletal osteosarcomas, such as those of the spleen, stained for vimentin (3/4) and actin (3/4) but not for desmin (0/4).¹¹ In some human salivary gland carcinosarcomas, the osteosarcoma component stained for cytokeratin, S-100, and vimentin but not for desmin, suggesting a myoepithelial origin.⁴ In other human salivary-gland carcinosarcomas, the osteosarcoma component appeared to have arisen from a separate cell line, staining only for vimentin but not for keratin, epithelial membrane antigen, S-100, or glial fibrillary acidic protein.² This evidence supports the undifferentiated pluripotential theory. The pluripotential theory also explains how a bony tumor could arise in a tissue that does not contain bone.¹ The positive actin reactivity in our case suggests a myogenic cell origin.

There are numerous types of canine salivary-gland tumors, the majority of which are malignant. Osteosarcoma of the salivary gland, like other extraskeletal osteosarcomas, appears to be an especially aggressive neoplasm. The cell of origin of these tumors is uncertain given the variety of immunohistochemistry results.

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