Case Report

Malignant Mixed Tumor of Salivary Gland in a Dog

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Abstract: A tumor was observed in the left mandible of a 3-year-old male Shih-Tzu dog. Histopathology revealed neoplastic alveolar proliferation of round cells, sarcomatoid proliferation of round to spindle-shaped cells and an existing parotid gland tissue around the tumor. A cancellous bone framework was also seen throughout the tumor. The tumor cells in the sarcomatoid area were positive and weakly positive for vimentin and cytokeratin, respectively, demonstrating their myoepithelial character. We diagnosed this tumor as a malignant mixed tumor of the salivary glands, because of the location of the tumor, its invasiveness into the surrounding tissue and the identification of both epithelial and myoepithelial tumor cells. (J Toxicol Pathol 2006; 19: 147–150)

Key words: salivary gland, canine, mixed tumor, osseous tissue

Primary neoplasms of the salivary glands are uncommon in domestic animals1–3, especially dogs, and have been reported in aged animals3. Most salivary gland tumors are diagnosed as carcinomas and sometimes as mixed tumors in domestic animals2–4. They are predominantly observed in the parotid gland in dogs3. Malignant mixed tumors comprise 2.6 to 4.2% of all canine salivary gland neoplasms1,3. Histopathologically, mixed tumors of the salivary glands consist of epithelial and myoepithelial components, both showing neoplastic proliferation and enchondral or membranous ossification may be seen3. We had a chance to examine an uncommon salivary gland tumor in a young adult dog. In this case, neoplastic cells derived from epithelial and myoepithelial cells were observed with considerable bone formation. This report describes the histopathological characteristics of the malignant mixed tumor of the salivary gland.

A 3-year-old male Shih-Tzu dog showed swelling of the left mandible and was referred to a veterinary hospital. A mass was found in the left mandibular subcutis, and it showed radiopacity but no continuity to the jawbone (Fig. 1). The mass (2×3×3 cm) was hard and solid, well demarcated from the surrounding tissues, and was light gray in color with brown patches. It was surgically removed in a veterinary hospital and submitted for histopathologic examination. The animal has shown neither recurrence nor occurrence of other tumors and was alive more than 4 years after the surgery.

After fixation with 10% neutral-buffered formalin, the mass was decalcified with formic acid solution, cut into pieces, embedded in paraffin and then sectioned at 1.5 to 2 μm. The sections were stained with hematoxylin and eosin (HE) and with Alcian blue, pH 2.6 periodic acid by the Schiff method (AB-PAS) and examined by light microscopy. Immunohistochemistry was also conducted by the labeled streptavidin-biotin (LSAB) method (DAKO, USA) using monoclonal mouse anti-human pan-vertebrate conserved cytokeratin (BMA Biomedical AG, Switzerland), monoclonal mouse anti-human vimentin (YLEM, Italy), monoclonal mouse anti-human smooth muscle actin (SMA) (DAKO, Denmark), monoclonal mouse anti-human p63 protein5,6 (DAKO, Denmark) and porcine amelogenin and rat ameloblastin antibodies (both of which were generated by Uchida et al.7,8) as the primary antibodies. The specificity of the immunoreactions was verified by staining negative and positive control specimens.

This tumor showed three distinct features: an area with alveolar proliferation, an area with sarcomatoid proliferation, and bone tissue involving cartilage tissue. The sarcomatoid area was located almost in the center of the tumor and was surrounded by the alveolar area. A cancellous bone structure was formed like a framework throughout the tumor. Normal parotid gland tissue was in close contact with the tumor but showed no image suggesting transition to the tumor (Fig. 2).

The alveolar area was composed of round tumor cells containing abundant clear or eosinophilic cytoplasm, and duct-like structures were also partially observed in this area (Fig. 3). Mitotic figures were observed scarcely. This type of tumor cell proliferated invasively into the surrounding
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1. Radiographs showing the salivary gland tumor.

2. Histological section highlighting the tumor tissue.
Fig. 1. Radiograph of the lower jaw. The mass was not continued with the jawbone.

Fig. 2. Low magnification showed three types of tissue: an alveolar area (open arrowheads), a sarcomatoid area (solid arrowheads) and bone tissue (asterisks). There was also normal parotid gland tissue (arrows) around the tumor. HE. \( \times 13 \).

Fig. 3. Duct-like structures were observed in the alveolar proliferation area. HE. \( \times 200 \).

Fig. 4. Tumor cells in the alveolar area proliferated invasively into the surrounding tissues. HE. \( \times 37 \).

Fig. 5. Round to spindle-shaped tumor cells in the sarcomatoid area contained abundant eosinophilic cytoplasm. HE. \( \times 213 \).

Fig. 6. Round to spindle-shaped tumor cells in the sarcomatoid area were positive for vimentin. \( \times 300 \).

Fig. 7. Round to spindle-shaped tumor cells in the sarcomatoid area were weakly positive for cytokeratin. \( \times 300 \).

Fig. 8. Bone tissue was composed of mature bone trabecula involving osteoblasts and osteoclasts with no atypia. HE. \( \times 121 \).
tissues (Fig. 4). Immunohistochemistry showed that these tumor cells were strongly positive for cytokeratin but negative for vimentin, amelogenin and ameloblastin. In addition, the duct-like structures frequently contained eosinophilic secretions. The eosinophilic secretions were stained blue by AB-PAS staining and exhibited a staining behavior similar to that of the secretions in the duct of the existing parotid gland.

The sarcomatoid area was composed of a solid proliferation of round to spindle-shaped tumor cells containing abundant eosinophilic cytoplasm, and mitotic figures were frequently observed (Fig. 5). Immunohistochemistry showed that these tumor cells were positive for vimentin (Fig. 6) and weakly positive for cytokeratin (Fig. 7), but were not stained by either SMA or p63 protein, myoepithelial cell markers.

The bone tissue was composed of mature bone trabecula involving osteoblasts and osteoclasts with no atypia (Fig. 8). It made up a framework throughout the tumor, but was not continuous to the lower jawbone. This bone tissue was closely similar to that found in common mammary benign mixed tumors.

This case exhibited two neoplastic proliferation patterns, alveolar and sarcomatoid, with a large amount of bone tissue formation. Based on the location of the tumor and the nature of its growth involving bone development, the possibility of an odontogenic tumor was suggested as a differential diagnosis. This diagnosis was rejected, however, because the tumor was not continuous to the lower jawbone, and the tumor cells showed negative staining with amelogenin and ameloblastin, available antibodies to enamel proteins.

The alveolar area included duct-like structures containing secretions with a staining behavior similar to that of the intraductal secretions in the surrounding normal parotid gland tissue. These facts and the tumor location strongly suggested that the tumor was derived from the salivary gland. In addition, the tumor was considered to be malignant, since the tumor cells proliferated invasively into the surrounding tissues.

Normal myoepithelial cells are positively stained with both cytokeratin and vimentin. In this case the spindle-shaped tumor cells in the sarcomatoid area were positive for vimentin and weakly positive for cytokeratin as well, demonstrating that these cells were derived from myoepithelial cells, although there was no detectable positive reaction for SMA or p63 protein, both myoepithelial cell markers. Considering that the sarcomatoid area was located in the center of the tumor and covered with bone tissue, it was presumed that poor fixation or decalcification affected the reactivity of the tumor cells to the myoepithelial cell markers.

According to the WHO diagnostic criteria, both epithelium- and myoepithelium-derived tumor cells must be identified to make a diagnosis of a salivary gland mixed tumor, and when either type of cell becomes malignant, a diagnosis of malignant mixed tumor is established. We diagnosed this tumor as a malignant salivary gland mixed tumor because of the location of the tumor, the invasive nature into the surrounding tissue and the identification of both types of tumor cells as described above. This case occurred in a relatively young animal and involved a large amount of bone formation. Thus, it was a rare case.

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References


