



Case Report

Salivary gland carcinosarcoma in a dog

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Abstract

Salivary gland tumors are uncommon in domestic animals, whereas salivary carcinosarcomas are very rare in the dog. A 15-year-old mongrel bitch was diagnosed with carcinosarcoma of the submandibular salivary gland extending into the adjacent muscular tissues and the jugular vein. The tumor displayed two distinct areas, one portion with sarcomatous neoplastic cells with bone and cartilage differentiation, and other areas with a pleomorphic carcinomatous tissue. The epithelial and mesenchymal nature of neoplastic cells were confirmed by immunohistochemistry. Surgery and chemotherapy treatments are discussed.

Key Words: Carcinosarcoma, salivary gland, dog, immunohistochemistry.

Introduction

Salivary gland tumors are uncommon in dogs and cats with an overall incidence of 0.17% (3). Primary malignant epithelial tumors are the most frequently diagnosed (3, 9, 22). Salivary gland tumors include adenocarcinomas, carcinomas, adenomas, mixed tumors, (3, 9, 22), and rarely carcinosarcomas (16), malignant myoepitheliomas (5), and osteosarcomas (23).

In veterinary medicine, carcinosarcomas are more often diagnosed in the canine mammary gland (2), but they may also primarily arise from apocrine glands of the skin (1), thyroid gland (6, 17), ceruminous gland (15), skull (19), lung (18), uncertain origin in the lumbosacral region (14), and mandibular salivary gland (16). Salivary gland carcinosarcomas have also been reported in cats (4, 10). Aged dogs and cats are more often affected (3, 9, 19), and the tumor usually arises from the mandibular or parotid glands (3, 8, 22).

The histogenesis of carcinosarcoma is not clearly understood, and even their nomenclature is a matter of debate (11, 19). Nevertheless, classification of a given neoplasia as carcinosarcoma is based on the presence of two distinct malignant components, one epithelial or myoepithelial and the other mesenchymal,

i.e. development of carcinomatous and sarcomatous tissue in the same neoplastic process (2, 11). Considering that carcinosarcoma is very rarely reported as a primary tumor of the salivary gland in dogs, here we describe a case of carcinosarcoma of the mandibular salivary gland, which was thoroughly characterized by immunohistochemistry. In addition, we discuss the surgery and chemotherapy applied in this case.

Case report

A fifteen-year-old mongrel bitch was admitted at the Veterinary Hospital of the Universidade Federal de Minas Gerais (Belo Horizonte, Brazil) with a right cranio-ventral cervical enlargement of approximately 20 centimeters in diameter (Figure. 1A). The bitch underwent surgery and the invasive mass in submandibular region involving salivary gland was removed. Before surgery, 200 ml of serous-bloody fluid were drained from cystic area of tumor. The mass was firm, poorly mobile, highly vascularized with approximately 20 cm in diameter, and extended into adjacent tissues including muscular tissues and the jugular vein (Fig. 1B).

The tumor was submitted for histopathology, and representative samples of the neoplastic tissue

were fixed by immersion in 10% buffered formalin, processed for paraffin embedding, and stained with hematoxylin and eosin (HE). Three- μ m sections were stained by standard streptavidin-biotin immunoperoxidase method (LSAB+ Kit, Dako Corp., Carpinteria, CA) with the following primary antibodies: monoclonal mouse anti-human cytokeratin AE1/AE3 (Dako, dilution 1:50), monoclonal mouse

anti-vimentin (Dako, dilution 1:100). Negative control sections of the tumor lacked primary antibody, and in addition to internal controls (i.e. epithelial and mesenchymal tissues in the remaining normal tissues in the section), positive control tissue sections were include for each antibody.

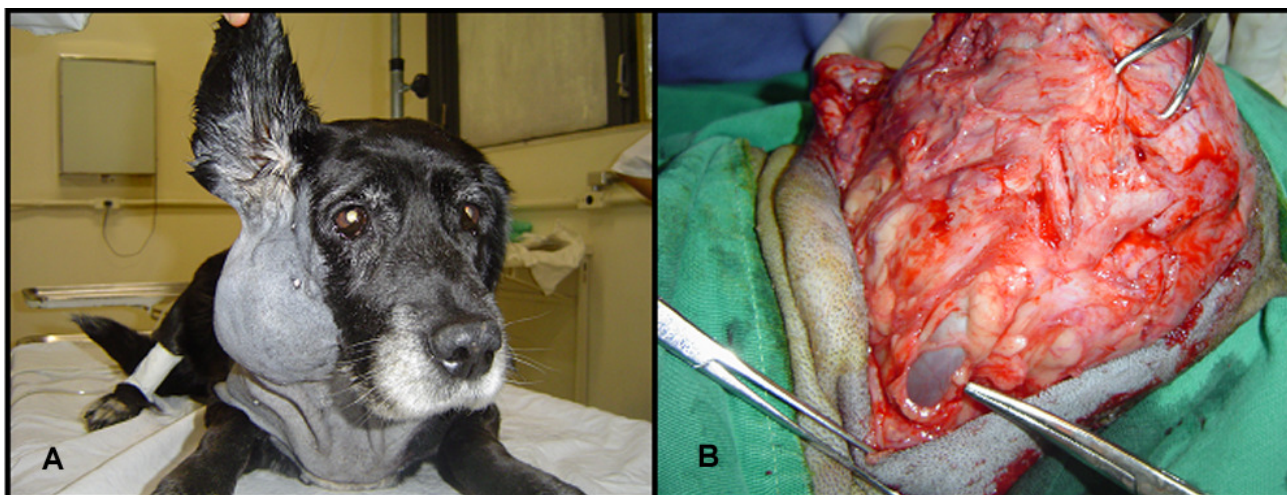


Figura 1: **A)** Dog. Cranio-ventral cervical enlargement of approximately 20 centimeters in diameter on right side. **B)** Dog in surgery. Invasive and firm mass in submandibular region involving salivary gland, muscular tissues and the jugular vein.

Grossly, the mass had 25 cm in diameter, was firm with an irregular and nodular surface, and on the cut surface, there were mixed areas of brownish and/or whitish color and firm or friable consistency. Histopathology revealed simultaneous proliferation of both epithelial and mesenchymal malignant components. The tumor displayed two clearly distinct areas partially separated by connective tissue. One portion presented neoplastic cells aligned along small, thin or globular, poorly calcified trabeculae of osteoid (Fig. 2A). The cells were oval to spindle shaped, and not had discernable cell boundaries and moderate, eosinophilic, fibrillar, and often vacuolated cytoplasm. The nuclei were round, oval, and had stippled chromatin and prominent nucleoli. In addition, there were multiple areas of necrosis, and presence of metaplastic cartilage and bone among myoepithelial cells. In other areas, carcinomatous cells with dense sheets of basophilic pleomorphic cells appearing to form acini, solid cords, and nests were supported by collagenous stroma (Fig. 2B). The neoplastic cells were polyhedral or rounded, with a high nucleus/cytoplasm ratio, they had a scant basophilic cytoplasm, and the nuclei were irregularly shaped with prominent nucleoli. High anisocariosis and high mitotic index were

observed, and bizarre mitotic figures were common. Immunohistochemistry results for vimentin and cytokeratin confirmed the presence of carcinomatous and sarcomatous components. The mesenchymal cells were strongly positive for vimentin (Fig. 3A), where most cells adjacent to osteoid was immunoreactive. Conversely, the majority of neoplastic glandular structures marked strongly for cytokeratin AE1/AE3 (Fig. 3B).

Following surgical resection of neoplastic mass without proper surgical margins, and the histopathological diagnosis of carcinosarcoma, chemotherapy was elected due a high risk of recurrence. Treatment started 15 days after surgery with Carboplatin (300 mg/m²) administered intravenously at 21 days/cycle, 3 cycles. The bitch presented no significant clinical changes during chemotherapy, without side effects caused by the cytostatic drug. However, the chemotherapy was interrupted due to the owner's decision. There was recurrence of neoplastic growth in the cervical region at the site of the previous surgical exeresis. The owners then elected euthanasia. The time of survival of this animal was 180 days. The owner did not authorize a necropsy.

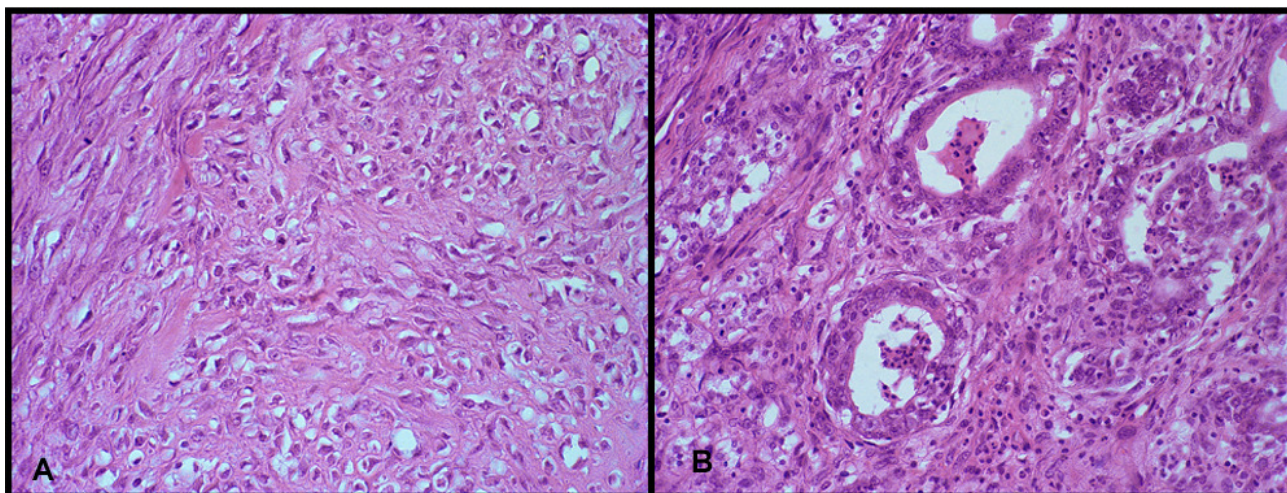


Figura 2: Dog. Carcinosarcoma in salivary gland. A) Malignant proliferation of mesenchymal cells with oval to spindle shape aligned along poorly calcified matrix osteoid. B) Section with area the malignant proliferation of cell epithelial forming acini and solid nest supported by collagenous stroma. HE, 400x

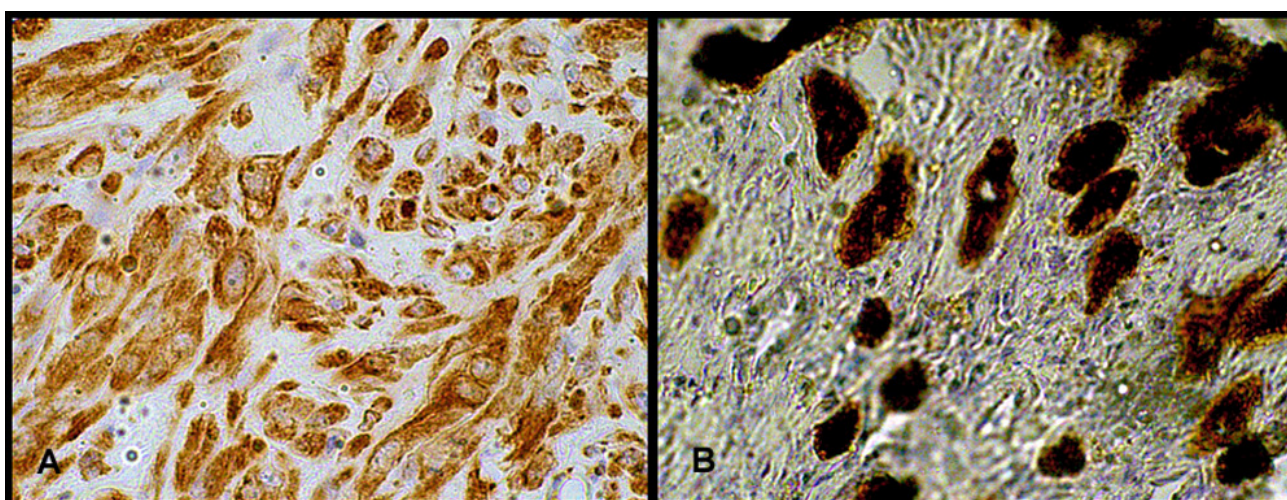


Figura 3: Dog. carcinosarcoma in salivary gland. A) Section from the mesenchymatous zone with a sarcomatous population showing immunoreactivity for vimentin (brown). B) Carcinosarcomatous zone with a squamous pater expressing immunoreactivity for cytokeratin (brown), adjacent mesenchymal cells without marking . Streptavidin-biotin peroxidase. 400x.

Discussion

Benign mixed tumor is most common neoplasm of gland salivary human (13), but it is uncommon dogs (9). Conversely, malignant mixed salivary gland tumor refers to carcinoma in pleomorphic adenoma (9, 11), which is a tumor characterized by a malignant epithelial component in a previously pleomorphic adenoma, and it has been described in dogs (3, 9, 20, 21). However, true carcinosarcoma is very rare in dog and cats (3, 9), and this case is only the second case report of salivary gland carcinosarcoma in a dog that was confirmed by immunohistochemistry (16). Carcinosarcoma is also considered a rare salivary gland neoplasia in man (11).

The diagnosis of carcinosarcoma in this case was based on the presence the two malignant components, one epithelial or myoepithelial and another mesenchymal. These morphological findings

were further characterized by immunohistochemistry, with sarcomatous and carcinomatous components being immunoreactive for vimentin and cytokeratin, respectively, as previously described (11, 16). Immunohistochemistry is extremely important for accuracy of the diagnosis of carcinosarcoma, supporting the differential diagnosis with other neoplasms (6, 17, 19). Other neoplasms that should be considered in the differential diagnosis includes malignant mixed tumor (20), spindle cell carcinoma, teratoma (19), and osteosarcoma, which has been reported as a primary neoplasm in salivary gland (23).

Our study reports a case of salivary gland carcinosarcoma in a dog with 15-year-old, without clinical manifestations other than local swelling, which is similar to other reported cases of salivary gland tumors (3, 8). Metastases were not clinically identified but the necropsy was not performed in this case. Malignant salivary gland neoplasms are usually

invasive, often recur after surgical excision, and can metastasize mostly to regional lymph nodes (3). Therefore, malignant salivary gland has a poor prognostic since the diagnosis is often delayed because of asymptomatic development of the tumor.

The indicated treatment of malignant salivary gland tumor is surgery resection. However, invasive tumors that involve adjacent vital structures complete resection is impractical. In these cases, radiotherapy is indicated as auxiliary treatment to promote local control of neoplasm and long-term survival (8). The use of chemotherapy as treatments of malignant salivary gland tumor has been not explored in dog. The media of survival of dogs treated with surgery and radiotherapy is about 550 days (8), however, the endurance of animals that suffer only tumor resection is 74 days (7) and association of surgery and chemotherapy has not been described in literature.

Malignant salivary gland tumor may have variable histology, biological behavior and responsiveness to systemic therapy. There is not any standard protocol of chemotherapy for these tumors, but platin-based treatment is often used in man (12). Since that the association of surgery and radiotherapy treatments was not possible, we opted for chemotherapy using carboplatin. The survival of this animal was 180 days, which is longer than the survival time of dogs treated with surgery only (7), but shorter than surgery associated with radiotherapy (8).

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