CLINICAL REPORT

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# Oral squamous cell carcinoma with bone invasion in two dogs - case report

## *Carcinoma de células escamosas oral com invasão óssea em dois cães – relato de caso*

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**ABSTRACT:** Squamous cell carcinoma (SCC) is the third most prevalent tumor in the oral cavity of dogs with middle to advanced age. This report describes the cases of dogs aged 8 and 13 years. The first animal presented sialorrhea with blood, hyporexia, emaciation, hypocorned mucous membranes, enlarged right submandibular lymph node, and, in the oral cavity, intense halitosis and nodosity in the right maxillary antimer, which was friable, blackened, adhered, and hemorrhagic, starting in the soft palate and infiltrating the hard palate. There was hypochromic microcytic anemia with the presence of anisocytosis and Heinz corpuscles, as well as thrombocytopenia, macroplatelets, leukocytosis due to neutrophilia, monocytosis with the presence of toxic neutrophils, and hyperproteinemia with hypoalbuminemia, decreased ALT, and urea. The patient underwent surgery to remove the nodule but returned for euthanasia days later due to aggressive tumor recurrence. The second animal presented masticatory dysphagia, anorexia, hypocorned mucous membranes, capillary filling time greater than 2 seconds, blowing in the mitral and tricuspid valves, and firm elevation in the lower part of the right mandible in the caudal mentonian region. Additional tests showed erythrocytosis, polychromasia, thrombocytosis, platelet aggregation, macro platelets, and increased ALT. Ultrasound examination showed renal alterations compatible with senile degeneration and/or nephropathy, nodulations in the spleen, prostate, and left testicle, and enlargement of the right adrenal gland. Initial anti-inflammatory and analgesic treatment was instituted, but he died. Necropsy and the histopathological examination of the animals showed a diagnosis of SCC with bone invasion, the latter being an uncommon fact.

**KEYWORDS:** oral neoplasia; canine; bone affected.

**RESUMO:** O carcinoma de células escamosas (CCE) é o terceiro tumor mais prevalente em cavidade oral de cães com idade média a avançada. Este relato descreve os casos de cães com 8 e 13 anos. O primeiro animal apresentava sialorreia com sangue, hiporexia, emaciação, mucosas hipocoradas, aumento de linfonodo submandibular direito e, na cavidade oral, halitose intensa e nodosidade no antímero maxilar direito, a qual se mostrava friável, enegrecida, aderida, hemorrágica, iniciando em palato mole e infiltrando-se em palato duro. Havia anemia microcítica hipocrômica com presença de anisocitose e corpúsculos de Heinz, além de trombocitopenia, macroplaquetas, leucocitose por neutrofilia e monocitose com presença de neutrófilos tóxicos, hiperproteinemia com hipoalbuminemia, diminuição de ALT e ureia. O paciente foi submetido a cirurgia para retirada do nódulo, mas voltou para eutanásia dias após por recidiva agressiva do tumor. O segundo animal apresentava disfagia mastigatória, anorexia, mucosas hipocoradas, tempo de preenchimento capilar maior que 2 segundos, sopro em valvas mitral e tricúspide e elevação firme na parte inferior da mandíbula direita em região caudal mentoniana. Nos exames complementares observaram-se eritrocitose, policromasia, trombocitose, agregação plaquetária e macroplaquetas, além de aumento de ALT. No exame ultrassonográfico, havia alterações renais compatíveis com degeneração senil e/ou nefropatia, nodulações em baço, próstata, testículo esquerdo e aumento de dimensão da glândula adrenal direita. Instituiu-se tratamento inicial anti-inflamatório e analgésico, porém ele veio a óbito. Na necrópsia e exame histopatológico dos dois animais o diagnóstico foi de CCE com invasão óssea, sendo este último achado fato pouco comum.

**PALAVRAS-CHAVE:** neoplasia oral; canino; comprometimento ósseo.

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## INTRODUCTION

Oral neoplasms in dogs occupy the fourth place among the neoplasms that most affect the species, with about 6% being malignant (Colombo, 2022). The prevalence of oral cavity tumors in dogs is higher in males with mid to advanced age, with melanoma being the most frequent malignant tumor, followed by mastocytoma, squamous cell carcinoma (SCC), and fibrosarcoma (Pereira *et al.*, 2021).

Oral SCC is a malignant neoplasm originating from keratinocytes in the stratified squamous epithelium of the oral mucosa. It is characterized by lesions that may be ulcerative or verrucous (Murphy; Bell; Soukup, 2020). It is also known as spinocellular carcinoma, squamocellular carcinoma, or epidermoid carcinoma due to its origin in keratinocytes (Lima; Gonçalves, 2023). It tends to present proliferative biological behavior with infiltrative capacity and low potential for metastasis that, when it occurs, mainly affects regional lymph nodes, bones, and lungs. The proposed causes or contributing causes for squamous cell carcinoma in veterinary species are numerous and include chronic exposure to air pollution, tobacco smoke, papillomavirus infections, flea collars, diet, prior exposure to radiation, and chronic mucosal and/or periodontal inflammation (Murphy; Bell; Soukup, 2020). Potential etiological factors include lack of skin pigmentation, chronic inflammatory diseases, burns, immunosuppression, and association with oncogenic papillomavirus (Lêmos, 2022).

The definitive diagnosis of SCC is histopathological, with microscopic examination of the injured tissue (Nagata; Macini; Ito, 2022). As a therapeutic modality, total surgical excision with a wide margin of safety is quite effective for disease remission when the tumor is diagnosed at an early stage and without evidence of metastases (Pipi *et al.*, 2016). However, in some cases where the neoplasm is in an advanced stage or complete surgical resection is not possible due to its anatomical location, it is necessary to associate adjuvant therapies, such as chemotherapy, radiotherapy, photodynamic therapy, electrochemotherapy, and/or cryosurgery (Lêmos, 2022). The prognosis of SCC in the oral cavity is usually reserved by the high local recurrence rate and anatomical location, which often limits therapeutic options (Lima, 2022).

This study aims to report two cases of oral SCC with bone invasion in the maxilla of patients treated at the Clínica Veterinária Escola da Universidade Federal de Santa Catarina (CVE/UFSC), Curitibanos campus, demonstrating the different behaviors of this neoplasm and its consequences to affected animals.

## CASE REPORTS

### Case 1

A castrated mixed breed dog, aged eight and 17.1 kg, was treated at the CVE/UFSC, Curitibanos *campus*. The tutors complained of the appearance of an oral nodule of hard consistency for about two weeks, with progressive growth, sialorrhea with blood, dysphagia, and emaciation. On physical examination, the animal presented a depressed state of consciousness, hypocorned mucous membranes, an enlarged right submandibular lymph node, and, in the oral cavity, intense halitosis and a nodosity in the right antimer (Figure 1), which was friable, blackened, adhered, starting in the soft palate and infiltrating the hard palate, hemorrhagic, and measuring approximately 10 cm x 6 cm. Pasty feeding was initially indicated, in addition to dipyrone (25 mg/kg BID VO for five days) and meloxicam (0.11 mg/kg SID VO for four days).

Subsequently, an incisional biopsy of the oral lesion was indicated for histopathological examination, but the tutor did not adhere to the recommendation. Thus, it was decided to perform a caudal maxillectomy due to the accelerated growth of the nodulation, which interfered with feeding, breathing, and quality of life. Preanesthetic tests, such as blood count, total plasma proteins (TPP), alanine aminotransferase (ALT), creatinine, albumin, alkaline phosphatase (ALP), and urea were performed for surgery. Radiography of the head and chest region was performed to outline the surgical bed better and look for metastases in pulmonary fields, respectively.

The erythrogram showed hypochromic microcytic anemia, with red blood cells of 4.4 x $10^6$/µL (reference: 5.7 to 7.4 x $10^6$/µL), decreased hemoglobin (7.2 g/dL; reference: 14.0 to 18.0 g/dL), hematocrit (23.3%; reference: 38 to 47%), mean corpuscular volume (MCV of 53.1 fL; reference: 63.0 to 77.0 fL), and the mean corpuscular hemoglobin concentration (HC) (30.9 g/dL; reference: 31.0 to 35.0 g/dL), with the presence of anisocytosis and Heinz corpuscles. The thrombogram showed thrombocytopenia (194 x $10^3$/µL; reference: 200 to 400 x $10^3$/µL) and macro platelets. The leukogram showed neutrophilic leukocytosis (18,761/µL; reference: 3,300 to 12,800/µL) and monocytosis (4,369/µL;

Source: Provided by the Laboratory of Clinic and Imaging of Small Animals (LACIPA/CVE/UFSC).

**Figure 1.** Macroscopic aspect of the ulcerated mass in the oral cavity of the first dog.

reference: 60 to 960/μL) with the presence of toxic neutrophils. Hyperproteinemia (8.5 g/dL; reference: 6 to 8 g/dL) was also observed, with mild hypoalbuminemia (2.19 g/dL; reference: 2.6 to 3.3 g/dL), a slight decrease in ALT (17 U/L; reference: 21 to 102 U/L), and urea (17.0 mg/dL; reference 21 to: 59.9 mg/dL).

Radiographs of the skull region (Figure 2) showed an increase in heterogeneous-looking volume in the mid and caudal third of the right maxillary bone, predominantly in soft tissues with interspersed radiolucent areas and without invasion of bone tissue. The thoracic radiographic evaluation showed no alterations or evidence of metastatic nodules in pulmonary fields.

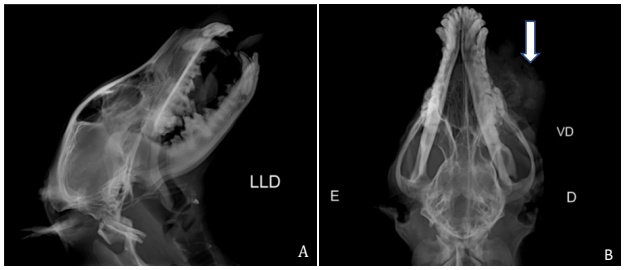
The surgical procedure was initiated with preanesthetic medication (PAM) using intramuscular morphine (0.3 mg/kg) and subsequent intravenous anesthesia using propofol (3 mg/kg), ketamine (1mg/kg), fentanyl (3 mg/kg), and lidocaine (2 mg/kg). Surgery began with a cutaneous and subcutaneous incision in the right labial commissure for better exposure of the nodule, followed by disclosure of the tissues adjacent to the nodule using Metzenbaum scissors, electric scalpel, and scalpel with blade No. 24. Using a hammer and osteotome, the maxillary osteotomy was performed from the first molar to the last, ending with the synthesis in a simple interrupted pattern in the hard palate, labial commissure, and skin. After surgery, amoxicillin with clavulanate (20 mg/kg VO BID for seven days), dipyrone (25 mg/kg VO QID for six days), tramadol (6 mg/kg VO QID for six days), and meloxicam (0.1 mg/kg VO SID for three days) were prescribed, in addition to the request for the use of Elizabethan collar. No histopathological evaluation was performed due to the tutor's non-adherence.

The patient returned to the CVE one week after the procedure, presenting a 0.4 cm fistula in the nasal plane due to the lack of use of the Elizabethan collar. Cleaning the lesion and antibiotic therapy with amoxicillin with clavulanate (20 mg/kg BID VO for five days) was recommended, in addition to dipyrone (25 mg/kg VO TID) if the animal presented pain. The animal returned two weeks later with the healing of the nasal plane fistula but with a recurrence of severe lesions at the nodulation site, with the invasion of contralateral nasal septum and upper airway obstruction, in addition to two itchy and ulcerated skin lesions in the dorsal portion of the nodule. The animal returned for euthanasia five days after the last evaluation, a decision taken considering the animal's well-being in the face of the aggressive return of the tumor and the consequences related to dyspnea caused by the invasion of the mass to the nasal septa.

The body was sent to the Veterinary Pathology Laboratory (LABOPAVE/CVE/UFSC) for necropsy. Samples were collected for histopathological analysis, confirming the origin of the mass in the oral cavity. Histopathological analysis showed areas with submucosal layer exposure with several islands of basophilic punctate material (suggestive of bacterial colonies). Polyhedral cells of eosinophilic cytoplasm were found in the mucosal and submucosal layers, often with indistinct cell boundaries and euchromatic nuclei, with marked pleomorphism and evident nucleoli. In addition, evident dyskeratosis in individual keratinocytes (Figure 3 A and B), reactive fibroblasts, and infiltrate composed of lymphocytes, macrophages, plasma cells, and neutrophils, as well as neovascularization and deposition of connective tissue were observed. Up to ten mitotic cells were observed in 2.37 $mm^2$. In addition, connective tissue destroyed and replaced adjacent bone tissue, and areas of mineralization and hemorrhage could be observed. Therefore, according to the characteristics observed in the histopathological examination, the suggestive diagnosis of squamous cell carcinoma with invasion in bone tissue of the maxillary bone is inferred and graded through histopathology as poorly differentiated.

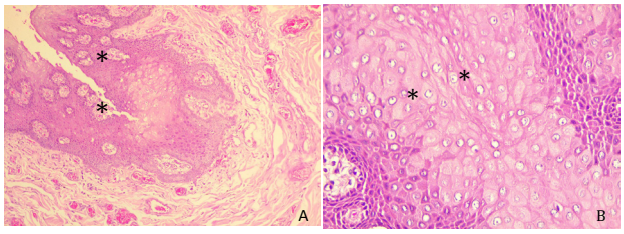
## Case 2

A mixed breed dog, not castrated, at 13 years of age, and 14 kg, was attended at the CVE/UFSC, Curitibanos *campus*, with the tutor's report that the animal had undergone dental extraction by a colleague due to a dental fracture, about a month before, but without signs of complete improvement since it remained with masticatory dysphagia. The animal was alert on




Source: Provided by the Laboratory of Clinic and Imaging of Small Animals (LACIPA/CVE/UFSC).

**Figure 2.** Radiographic images of the head region of the first dog: right laterolateral (A), ventrodorsal (B) projections; volume increase of heterogeneous aspect in the right maxilla (arrow).




Source: Provided by the Veterinary Pathology Laboratory (LABOPAVE/CVE/UFSC).

**Figure 3.** Histological mass section in the oral cavity of the first canine, male, mixed breed, eight years. **A:** Marked focally-extensive epithelial cell proliferation area is observed; the cells present dyskeratosis in the center (indicated by asterisks). HE staining, 100x magnification. **B:** A population of polyhedral cells with marked cellular pleomorphism (anisocytosis and anisocariosis) and individual dyskeratosis (indicated by asterisks) is observed. HE staining, 400x magnification.

physical examination, with a capillary filling time greater than two seconds and a murmur in the mitral and tricuspid valves, grades 4 and 3, respectively. Firm elevation was observed in the lower part of the right mandible, in the caudal mentonian region, approximately 3 cm in diameter. However, the animal did not allow a more detailed examination of the oral cavity due to aggressive behavior. Blood count, serum biochemistry (urea, creatinine, albumin, ALT, and ALP), abdominal ultrasound (US), and echocardiogram were requested. The tutor did not authorize the latter. Dipyrone (17 mg/kg TID VO until further recommendations), meloxicam (0.1 mg/kg SID for three days), and tramadol (2.8 mg/kg BID until further recommendations) were prescribed.

The blood count showed an increase in hematocrit (52.4%, reference: 38 to 47%), with polychromasia, mild thrombocytosis (563 x $10^3$/µL; reference: 200 to 500 x $10^3$/µL) with platelet aggregation, and the presence of macroplatelets. Serum biochemistry showed increased ALT (147.4 U/L; reference: 10-88 U/L) and ALP (217 U/L; reference: 20-156 U/L). Abdominal ultrasound indicated a decrease in renal length in relation to the aortic artery and images compatible with mineralization in the renal diverticulum region, indicating possible senile degeneration and/or nephropathy. Nodulations in the spleen, prostate, and left testicle, in addition to an increase in the size of the right adrenal gland, were also observed.

Upon return for oral cavity examination and biopsy, the animal presented anorexia for two days, apathy, and adipsia. Physical examination showed nervousness, depression, and hypocorned mucous membranes. Anesthesia was performed using methadone (IV, 0.5 mg/kg) and propofol (IV, dose effect). Inspection of the oral cavity showed an increase in volume in the right mandible region, with a reddish, non-ulcerated, and firm appearance, involving from the second premolar to the molars (Figure 4). Samples collected with dermatological *punch* incisional biopsy were sent for histopathological evaluation. Subsequently, an amino acid vitamin supplement was prescribed for nutrition and appetite stimulation. However, the animal died at home a few days later, and the body was sent to LABOPAVE/CVE/UFSC for necropsy.

Source: Provided by the Laboratory of Clinic and Imaging of Small Animals (LACIPA/CVE/UFSC).

**Figure 4.** Macroscopic aspect of the lesion in the right mandible to the evaluation of the oral cavity of the second dog, showing the increase in volume in the mandible and oral mucosa that covers the dental arches and periosteum (arrows).

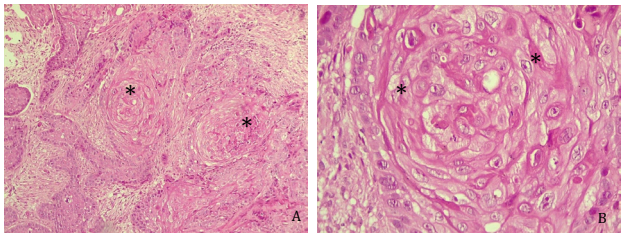
Histopathological analysis of the oral cavity mucosa and mandibular bone identified islands of polyhedral epithelial cells with eosinophilic cytoplasm, indistinct cell boundaries, nuclei with marked pleomorphism, and evident nucleoli, with keratin pearl formation and neoplastic cells interspersed in the connective tissue with 30 mitoses in 2.37 mm² (Figure 5), consistent with squamous cell carcinoma with bone infiltration, graded as well differentiated through histopathology.

## DISCUSSION AND CONCLUSIONS

The prevalence of oral cavity tumors in dogs is higher in males, usually at mid to advanced age (PEREIRA *et al.*, 2021), which matches the characteristics of the two reported animals, aged 8 and 13 years, respectively.

Anorexia, progressive weight loss, and halitosis in patients with oral neoplasms occur due to the patient's difficulty in grasping and chewing food due to pain and discomfort (Munday, 2016; Da Silva, 2023). These signs were present in both animals; in the first case, the animal also had intense halitosis. In addition, the first animal presented a larger mass and faster growth compared to the second dog, which, according to De Castro Cunha (2021), indicates a worse prognosis since tumor growth is directly linked to the rate of cell proliferation of neoplastic cells, with tissue invasion and metastasis.

SCCs are the most frequent neoplasms in dogs' oral cavities. They mainly affect the gums, lips, tongue, and palate but can also invade bone structures and metastasize to regional lymph nodes (Correa, 2022). It is believed that the primary factors involved in its formation in this location include chronic periodontal disease, ulcerations, and oral papillomatosis (Da Silva, 2023). In the first case, the animal presented a neoplasm with bone invasion in the upper region of the maxilla, which




Source: Provided by the Veterinary Pathology Laboratory (LABOPAVE/CVE/UFSC).

**Figure 5.** Histological section of mass in the oral cavity. **A:** Proliferation in polyhedral cell islands, with eosinophilic and indistinct cytoplasm (indicated by asterisks), is observed. 100x magnification. **B:** Individual keratinizing cells and concentric keratin lamellae are observed. The cells show marked cellular pleomorphism (indicated by asterisks). 400x magnification.

infiltrated the soft and hard palate. The second case demonstrated a smaller nodule in the lower region of the mandible but with no infiltration in the adjacent tissues, also having a history of tooth extraction due to dental fracture, which may be associated with the appearance of the neoplastic mass.

The macroscopic patterns of SCC are erythema, ulcer, plaque, and increased volume (Rosolem; Moroz; Rodigheri, 2012). Proliferative SCCs may present lesions of different sizes, from a few mm to several cm, ranging from firm and reddish plaques to papillary masses of various sizes and with cauliflower appearance. Its surface bleeds easily and is usually ulcerated (Silva, 2021). The reported cases had varied dimensions. In the first animal, the mass was hemorrhagic and ulcerated, and in the second, it was characterized as an increase in non-ulcerated reddish volume. SCC histology reveals the proliferation of epithelial cells, and its basic characteristics include squamous differentiation with keratinization, variable formation of horny pearls, and invasive growth. The invasion is demonstrated by a disturbance of the base membrane and extension into the underlying tissue, often accompanied by a stroma reaction. Angiolymphatic and perineural invasion are additional signs of malignancy (Barnes *et al.*, 2005; Pimentel, 2022). The first case presented the proliferation of granulation tissue interspersed with reactive fibroblasts and the cells separated by dense connective tissue. In the second case, classical features such as keratin pearl formations, moderately abundant stroma, and destruction of adjacent bone tissue were observed.

Bone invasion of the SCC is uncommon, with some reports of cranial invasion. Tomography showed neoplastic tissue with areas of mineralization and variable osteolysis of adjacent bone (Lojszczkyk *et al.*, 2021). Both cases discussed presented adjacent bone tissue by histopathological evaluation. However, tomography was not performed. Only radiography was performed in the first case, showing no evident bone involvement.

The treatment option of total nodule removal through maxillectomy was adopted in the first case. According to Pipi *et al.* (2016), mandibulectomy and maxillectomy are the main techniques for removing these oral tumors. However, as reported and according to the literature, the prognosis of oral SCC is reserved mainly due to the occurrence of relapse, as was the case with the first animal, thus decreasing the chances of treatment success. In the second case, the treatment aimed to stabilize the clinical condition of the animal to allow testing for the most assertive diagnosis, but the patient died before receiving the diagnosis and starting a specific treatment.

The analysis of the cases addressed highlights the complexity associated with oral cavity tumors with bone invasion in dogs, the difficult diagnosis of bone invasion of adjacent tissues, which in these cases was only completely elucidated after necropsy, the higher prevalence in males of middle to advanced age, and the importance of surveillance in certain population groups. It also indicates the need for further studies on bone invasion in oral neoplasms in dogs since few data are available on the subject. The decision to euthanize in the first case, motivated by the recurrence of the tumor and its respiratory implications, highlights the importance of considering the patient's well-being when managing these cases, emphasizing the need for therapeutic strategies aimed at efficacy and quality of life. Furthermore, this study highlights the importance of a multidisciplinary approach in managing oral cavity tumors in dogs, focusing on the need for future research and innovative therapeutic strategies to improve clinical outcomes and quality of life of these canine patients.

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