



CASE REPORT

Oral Squamous Cell Carcinoma with Lymph Node Metastasis in a 12 Years-Old Sphynx Female Cat

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Sfenks Irkı 12 Yaşındaki Dişi Bir Kedide Lenf Nodu Metastazlı Oral Yassı Hücreli Karsinom

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Öz

Bu raporda, 12 yaşında Sfenks ırkı dişi bir kedide lenf nodu metastazlı olan oral yassı hücreli karsinom (OYHK) olgusu tanımlanmıştır. Mandibular lenf nodu tamamen çıkarıldı ve diseke edildi (lenfadenektomi). Ağız mukozasındaki nekrotik-ülserli kitle ekstirpe edildi. Oral kitlede, atipik hücresel özelliklere sahip pleomorfik yassı epitel hücreleri, erozyonlar ve ülserler de gözlemlendi. Mandibular lenf nodunda belirgin atipik hücre özelliklerine sahip yassı epitel hücreleri bulundu. İmmunohistokimyasal incelemede neoplastik hücrelerin AE1-AE3 ve sitokeratin 5/6 için pozitif olduğu görüldü. Ağız mukozasında erozyon ve ülserlerle seyreden kronik gingivostomatitisli köpek ve kedilerin OYHK açısından da değerlendirilmesi gerektiğine dikkat çekmek amacıyla olgunun sunulması uygun bulunmuştur.

Anahtar kelimeler: Kedi, Metastaz, Oral yassı hücreli karsinom, Sfenks.

Abstract

In this report, a case of oral squamous cell carcinoma (OSCC) with lymph node metastasis was described in a 12 years-old Sphynx female cat. The mandibular lymph node was totally removed and dissected (lymphadenectomy). The oral necrotic-ulcerated mass was extirpated. In the oral mass, pleomorphic squamous epithelial cells with atypical cellular features, erosions and ulcers were also observed. Squamous epithelial cells with prominent atypical cell features were found in the mandibular lymph node. Immunohistochemical examination revealed that neoplastic cells were positive for AE1-AE3 and cytokeratin 5/6. It was found appropriate to present the case in order to draw attention to the fact that dogs and cats with chronic gingivostomatitis with erosions and ulcers on the oral mucosa should also be evaluated in terms of OSCC.

Keywords: Cat, Metastasis, Oral squamous cell carcinoma, Sphynx.



Introduction

Oral squamous cell carcinoma (OSCC) is cancer of the lining of the oral cavity, including the gingiva (gums), tongue, palate and tonsils. It is the most common oral cancer in cats. The most common sites of metastasis are lymph nodes of the head and neck and the lungs (Bilgic et al 2015, Munday et al 2017, Zaccone et al 2022, Noall et al 2023). OSCC can occur in any site of the oral cavity, but the lingual/sublingual area, the mandible, and maxilla show higher prevalence (Bilgic et al 2015, Noall et al 2023).

As in dogs, feline oral cavity squamous cell carcinomas are locally invasive and have low metastatic potential. Tumors can extend into the bones of the upper or lower jaw. Several factors have been described that can lead to the development of oral squamous cell carcinoma in cats, including contact with carcinogens in flea collars, topical tick and flea medications or grooming behavior (Bertone et al 2003, Wingo 2018, Noall et al 2023). Additionally, consumption of canned cat food and canned tuna has been linked to the development of this disease (Bertone et al 2003, Zaccone et al 2022, Noall et al 2023).

In a study about oral cavity lesions in dogs and cats (Mikiewicz et al 2019), the researchers have stated that they have found malignant tumors in dogs and cats constituted 32.06% (109/340) and 21.91% (32/146) of the lesions, respectively, with high-grade melanoma in dogs and squamous cell carcinoma in cats being the most common. In dogs, the most frequent malignancy was melanoma (35.78% of all malignant tumors; 39/109). Other commonly diagnosed malignancies were squamous cell carcinoma (26.61%; 29/109), fibrosarcoma (12.84%; 14/109) and osteosarcoma (10.09%; 11/109). In cats, malignant tumors constituted 21.92% (32/146) of the feline oral cavity tumors. The most common malignancy of the feline oral cavity was squamous cell carcinoma (75% of all malignant tumors; 24/32), followed by fibrosarcoma (12.5%; 4/32) (Mikiewicz et al 2019).

In another study investigating OSCC in cats (Ozturk-Gurgen et al 2022a), it was reported that the most affected life stage was determined as adult (n = 14/44; 31.81%) with an average age of 10.07 years, the majority of cases (n = 37; 84.04%) were mixed breeds, and the rest were Iranian (n = 5; 11.36%) and Turkish Angora (n = 1; 2.27%) breeds. The authors stated that the most affected areas were mandible (n = 10; 22.72%) and tongue (n = 8; 18.18%).

In this case report, we aimed to share the clinical, radiological, histopathological and immunohistochemical findings of OSCC detected in the oral mucosa and metastasis to the lymph node in a 12-year-old sphinx cat.

Case presentation

Informed consent was obtained from the animal owner. Owners' consent was obtained for the procedures undertaken and the use of the data for research purposes. The case material of the study consisted of a 12-year-old neutered female sphynx cat. The owner noticed a swelling in the cat's right mandibular area and a bloody saliva from the mouth about 10 days ago and was brought to the Kyrgyzstan-Turkey Manas University Veterinary Faculty Clinic for examination.

Clinical, laboratory and radiographic findings

On examination, it was noted that the subcutaneous lymph node in the right mandibular region was enlarged and had a hard consistency (Figure 1A). Large necrotic-ulcerated areas were also observed on the buccal mucosa and gingiva on the right side of the mouth (Figure 1B). The radiographic examination did not reveal any pathology in the bones except for the irregular appearance of molar teeth in the mandibular region on the right side. Calcification areas were observed especially in the area of the lesion (Figure 1C).

After general controls were performed, it was decided to remove the masses in the mouth and mandibular region by surgery. The results of blood analyze were within normal limits. Anesthesia was administered with Xylazine hydrochloride (1 ml/10 kg, Vetaxyl, Vetaş, Istanbul, Türkiye) and ketamine hydrochloride (10 mg/kg, Ketamidor, Vetaş, Istanbul, Türkiye). For the surgery, the mandibular area was shaved and disinfected. An oval incision was made into the skin. The mandibular lymph node was separated from the surrounding tissues and totally removed and dissected (lymphadenectomy) (Figure 2A). Later, the skin with simple separate sutures. The oral necrotic-ulcerated mass was removed and molar teeth were extracted (Figure 2B). Postoperatively, ceftriaxone sodium (Novosef 1 g, Sanofi, Istanbul, Türkiye) was used for 7 days against secondary infections.

Macroscopic findings

The surgically removed mass and lymph node were sent to the pathology laboratory for diagnostic examinations. The mandibular lymph node was 1,5x1x0,8 cm in size, lobular structure and had a firm consistency (Figure 3A). The cut-surface was greyish-white foci were observed (Figure 3B). It was noted that there was no tissue integrity in the mass taken by mouth, and therefore the size of the masses taken could not be measured. It was noticed that some areas of this mass had yellowish structures with red colored bleeding, necrotic and ulcerated structures and a fragmented appearance.

The tissues were fixed in 10% neutral buffered formalin solution. Fixed tissues were processed routinely and blocked in paraffin. Then, 4-5 micron thick sections

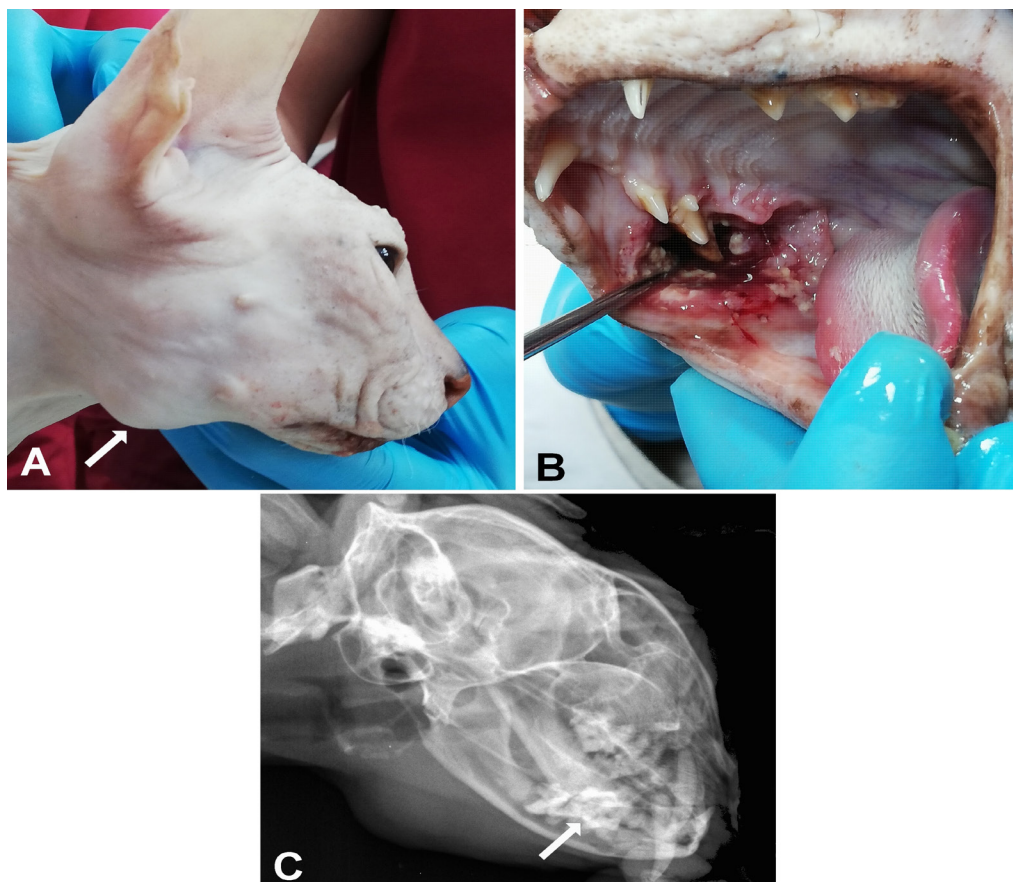


Figure 1. A- Enlarged lymph node (arrow) on the right mandibular region, B- Oral squamous cell carcinoma, necrotic-ulcerated appearance on right mandible and buccal mucosa, C- In the radiographic image, irregular appearance of molar teeth (arrow) in the mandibular region on the right side.

were taken from the samples in paraffin blocks with a microtome to normal and silane-coated adhesive slides. Sections were stained with hematoxylin-eosin (H&E) and immunohistochemically. The samples taken from adhesive slides were immunohistochemically stained with cytokeratin AE1-AE3 (1/200 dilution, DAKO -M3515, CA,

USA) and Cytokeratin 5/6 (1/100 dilution, Thermo-MS1814, CA, USA). Secondly, biotinized anti-mouse antibody (1/100 dilution, Boster bio-BA1007, CA, USA) was applied and incubated for 30 min. After washing, it was treated with Peroxidase enzyme conjugated streptavidin (Standard Vectastain Elite ABC Kit, PK-6100, Vector Labor. Inc, CA,

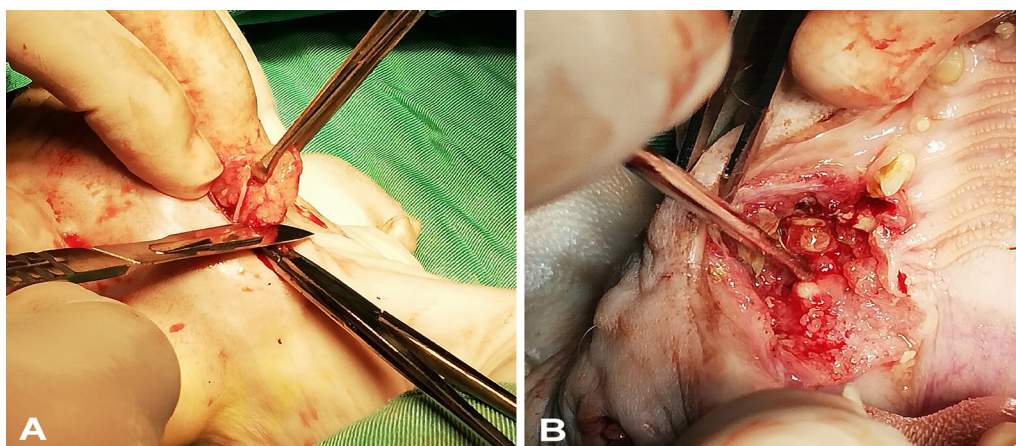


Figure 2. A- Removal and dissection of the mandibular lymph node (lymphadenectomy), B- Removal of necrotic-ulcerated mass in the mandibular and buccal region.



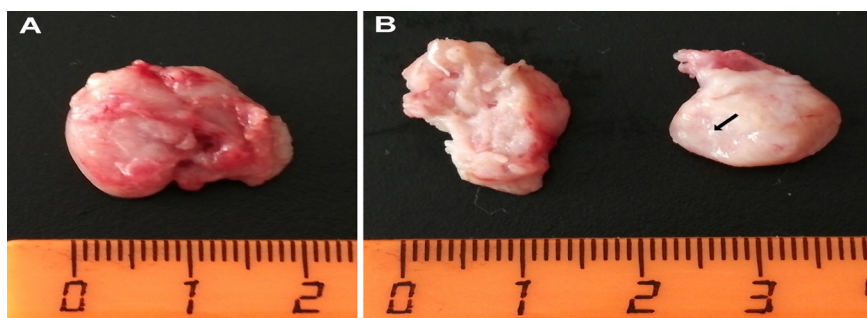


Figure 3. A- General appearance of an enlarged mandibular lymph node, B- Greyish-white foci (arrow) on the cut-surface of the mandibular lymph node.

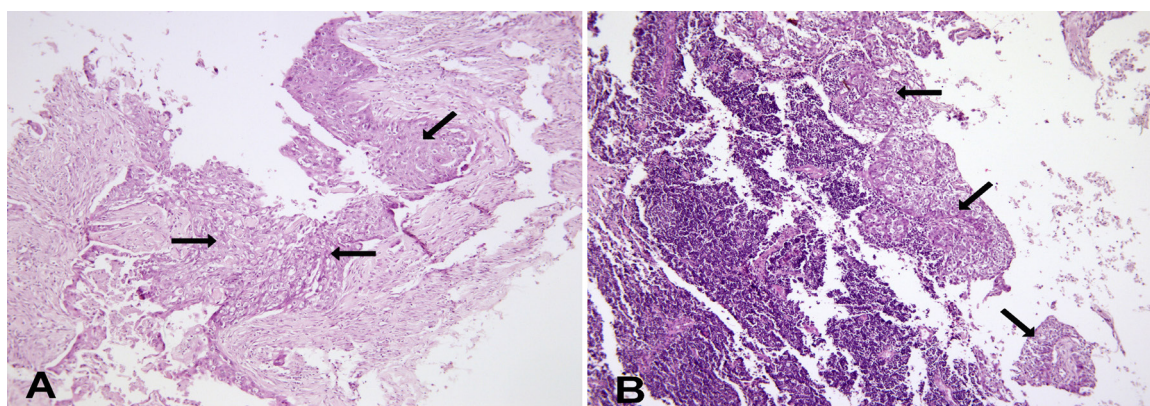


Figure 4. A- Appearance of neoplastic squamous cells (arrows) in the desmoplastic stroma, oral mucosa, H&E, x100, B- Metastatic neoplastic squamous cells (arrows) in the lymph node, H&E, x100.

USA) for 30 min. Washed with TBS. Finally, the reaction was colored by applying the peroxidase substrate [3-amino-9-ethylcarbazole (AEC), (SK-4200), Vector Labor. Inc, CA, USA]. Gill's (III) hematoxylin was used for the base and the slides were covered with aqueous mounting medium. All samples were examined under a light microscope.

Microscopic findings

Microscopic examination revealed erosions and ulcers caused by degeneration, necrosis and desquamation of

the squamous epithelial cells of the oral mass. In addition, inflammatory cells consisting mostly of neutrophil granulocytes were observed. Along with these changes, tumoral changes with atypical cell features such as anisonucleosis, anisocytosis and hyperchromasia were observed in the pleomorphic squamous epithelial cells (Figure 4A). In the mandibular lymph node, irregular tumoral foci consisting of squamous epithelial cells with prominent atypical cell features were found in the lymphoid tissue (Figure 4B). Hydropic and vacuolar degeneration

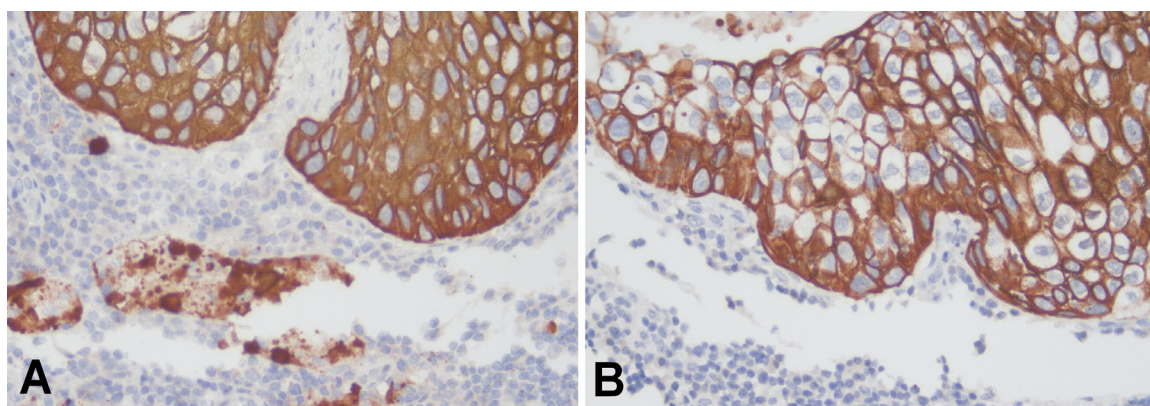


Figure 5. Neoplastic squamous epithelial cells positive in lymphoid tissue, A- AE1-AE3, x400, B- Cytokeratin 5/6, x400.





was observed in some of the tumoral cells both in the oral mucosa and in the lymph node. Keratinization and globe corne were not observed in the tumor foci formed by squamous cells with atypical changes in the oral mucosa and lymph node. Immunohistochemical examination revealed that cytoplasmic staining of neoplastic cells were positive for AE1-AE3 and cytokeratin 5/6 (Figures 5A and 5B).

Discussion

Squamous cell carcinoma (SCC) is a malignant neoplasm of epidermal cells in which the cells show differentiation to keratinocytes. It is one of the most common malignant skin tumors of all domestic animals, including chickens. There are several factors that are associated with the development of SCC, including prolonged exposure to ultraviolet light, lack of pigment within the epidermis at the sites of tumor development, and lack of hair or a very sparse hair coat at the affected sites. Therefore, geographic location and climate (ultraviolet light exposure) and anatomic location (conjunctiva, vulva, perineum) will greatly influence the incidence (Goldschmidt and Goldschmidt 2017). SCCs are the most common oral neoplasm of cats, horses, and the production animal species. They are the second most common malignant oral neoplasm of dogs. In humans, SCCs represent 95% of all oral neoplasms, and tobacco and alcohol consumption are considered the most common cause of oral SCCs in developed countries. However, poor oral hygiene and an inadequate diet also increase neoplasia risk (Bertone et al 2003, Munday et al 2017, Noall et al 2023).

Rising number of published studies indicates that *Felis catus* papillomaviruses (FcaPVs) exhibit mucosal tropism, being consistently detectable in a subset of OSCC of cat and playing a co-causative role in the development of these tumors (Munday et al 2017, Altamura and Borzacchiello 2023). Ozturk-Gurgen et al (2022b) reported that they obtained positive intracellular dark brown immunoreaction by immunohistochemistry against papillomaviruses in 5 of 32 OSCC cases.

Feline OSCCs most commonly develop within the mandibular, maxillary, and sublingual regions and neoplasia develops within these three locations at approximately equal rates (Bilgic et al 2015, Munday et al 2017). The average age for neoplasm development is around 13 years with a range of 1.5–22 years. No sex, coat color, hair length, or breed predispositions have been identified (Bertone et al 2003, Munday et al 2017). In the present case, OSCC was found in the mandibular region of a 12-year-old sphynx cat. The findings in our case were consistent with the information given by the investigators. However, we could not find any information and report on the detection of OSCC in sphynx cats.

Owners of dogs and cats most frequently become aware of an oral tumor by observing a mass. Other clinical signs can include halitosis, excessive salivation, dysphagia, hemorrhage, displacement or loss of teeth, facial swelling, anorexia, weight loss, or regional lymphadenopathy (Munday et al 2017). This tumor often clinically resembles a non-healing ulcer and mimics foreign body reactions or eosinophilic ulcers (Wingo 2018, Mikiewicz et al 2019). Feline oral SCCs cause necrosis of surrounding epithelial and connective tissues, which is often worsened by ulceration and secondary bacterial infection. Cats are almost invariably euthanized due to local disease resulting in anorexia, dysphagia, or dyspnea rather than the development of clinically significant metastases (Munday et al 2017). Similarly, in our case, increased bloody salivation and swelling in the right mandibular region were noticed by the owner and the animal was brought to our clinic for examination. On clinical examination, large necrotic-ulcerated areas were observed on the buccal mucosa and gingiva on the right side of the mouth. However, researchers reported that they diagnosed necrotic glossitis in a mass surgically removed from a cat's tongue with suspected tumor (Hatipoglu et al 2021). Considering both of these conditions, the importance of histopathological evaluation of necrotic and ulcerated lesions observed in the oral mucosa and tongue becomes obvious.

On microscopic examination, tumoral changes with atypical cell features such as anisonucleosis, anisocytosis and hyperchromasia were observed in the pleomorphic squamous epithelial cells in oral mucosa and in the lymph node. These histopathological changes were similar to those reported by the researchers in OSCC (Mikiewicz et al 2019, Ozturk-Gurgen et al 2022b, Muñoz-Duque et al 2023). However, glob corne and keratinisation observed in well-differentiated OSCCs were not detected in this case and therefore this case was considered as a poorly differentiated form of OSCC (Goldschmidt and Goldschmidt 2017, Munday et al 2017, Kutlu et al 2022). The fact that the changes in OSCC observed in the oral mucosa were also observed in the mandibular lymph node supports the researchers who reported that OSCC may metastasis to regional lymph nodes (Herring et al 2002, Mikiewicz et al 2019).

In presented case, immunohistochemical examination revealed that cytoplasmic staining of neoplastic cells were positive for pan-cytokeratin, clon AE1-AE3 and cytokeratin 5/6. Many epithelial clones exhibit positive expression for AE1-AE3. However, cytokeratin 5/6 is more commonly used in the diagnosis of squamous cell tumors and is evidence that the carcinoma in this case is squamous cell carcinoma (Chu and Weiss 2002).

There are numerous treatment options for oral SCCs, including surgical excision, radiation therapy, chemotherapy,



and photodynamic therapy, however the prognosis is poor in most of the cases, leading to death or euthanasia (Munday et al 2017, Altamura and Borzacchiello 2023). Despite multimodal treatment, the prognosis for this fast-growing, invasive tumor remains grave. This is mainly due to the fact that OSCC in cats is not detected until it has reached an advanced stage. Thus, early diagnosis is crucial for improving the survival rate (Bilgic et al 2015, Zacccone et al 2022).

Conclusion

In this case presentation, we aimed to share the clinical, radiological, histopathological and immunohistochemical findings of OSCC detected in the oral mucosa and metastasis to the lymph node in a sphinx cat. It was found appropriate to present the case in order to draw attention to the fact that dogs and cats with chronic gingivostomatitis with erosions and ulcers on the oral mucosa should also be evaluated in terms of OSCC and to contribute to the field of veterinary medicine.

Conflict of Interest

Authors declares that there are no conflicts of interest related to the publication of this article.

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Author Contributions

Motivation / Concept: FH, AT; Design: FH, MFB, IS; Control/Supervision: AT, AR; Data Collection and Processing: FH, AT; Analysis and Interpretation: AT, MFB; Literature Review: FH, MFB; Writing the Article: FH, AR, IS; Critical Review: FH, AR, IS

Ethical Approval

Informed consent was obtained from the animal owner. Owners' consent was obtained for the procedures undertaken and the use of the data for research purposes.