

Adenocarcinoma Involving the Tongue and the Epiglottis in a Horse

Fulvio LAUS^{1)*}, Giacomo ROSSI¹⁾, Emanuele PAGGI¹⁾, Matteo BORDICCHIA²⁾, Margherita FRATINI¹⁾ and Beniamino TESEI¹⁾

¹⁾School of Veterinary Medical Sciences, University of Camerino, Via Circonvallazione 93–95, 62024, Matelica (MC) Italy

²⁾Practitioner, Clinica Veterinaria San Biagio, Via Monsignor O. Romero 31, 60027, S. Biagio di Osimo (AN), Italy

(Received 13 August 2013/Accepted 13 November 2013/Published online in J-STAGE 27 November 2013)

ABSTRACT. Tumors involving the oral cavity of the horse are uncommon. No cases of equine adenocarcinoma on the dorsum of the tongue have been reported in the literature. We report a case of adenocarcinoma located on the dorsum of the posterior one-third of the tongue in a 29-year-old gelding with severe dysphagia. Endoscopy revealed an epiglottis involvement, and histology was consistent with adenocarcinoma arising from minor salivary glands, which was associated with a severe fungal colonization of affected tissues. The goals of this report are to present an uncommon case of dorsum of the tongue-associated neoplasia and to highlight the association with atypical fungal colonization, to review the literature and to discuss possible clinical approach and prognosis.

KEY WORDS: adenocarcinoma, base of tongue, equine, fungal infection, minor salivary glands.

doi: 10.1292/jvms.13-0417; *J. Vet. Med. Sci.* 76(3): 467–470, 2014

A 29-year-old gelding was presented to us, because of weight loss and difficulty eating over a 4 month period. The owners also reported that the horse drooled saliva from its mouth throughout the day.

Clinical examination revealed that the horse had a poor body condition, was depressed and was slightly dehydrated. The horse's heart rate, breathing, temperature and submandibular lymph nodes were normal. A venous sample of blood was taken, but its blood chemical parameters, electrolytes and red and white blood cell counts were normal, with the exception of a slight increase in neutrophils. Negative results were also found in a blood gas analysis performed on arterial blood.

When the horse was fed, he tried to eat, but after several chews, the food (both hay or concentrates) flowed from its mouth mixed with a large amount of saliva. The horse appeared to be able to swallow normally. A speculum was applied to the mouth after sedation (acepromazine, 0.02 mg/kg IV followed after 15 min by butorphanol, 0.02 mg/kg IV, acepromazine, 0.02 mg/kg IV, and xylazine, 0.2 mg/kg IV), and an oral examination performed. A careful inspection of the oral cavity revealed an abnormal lack of tissue on the left side of the dorsal aspect of the base of the tongue causing a sort of groove measuring about 12 cm in length, 2 cm in width and 2 cm in depth, which contained malodorous and roughly chewed food.

Oral endoscopy revealed that the floor of the lesion appeared congested with a granular appearance and contained a scattering of by small ulcerative areas (Fig. 1). Tongue

palpation did not cause pain and revealed that the lesion boundary had a firm consistence. Samples of tissue were taken using uterine biopsy forceps. No significant teeth alterations were found.

Ultrasonography of the tongue was performed using the intermandibular space as the acoustic window (Fig. 2).

Endoscopy of the upper airways revealed no abnormalities of the soft palate, but a small amount of red colored tissue was found that protruded from the right dorsal aspect of the epiglottis (Fig. 1). This tissue was sampled, in this case using transendoscopic biopsy forceps passed through the work channel of the scope. Endoscopy of the guttural pouches revealed normal results, with the exception of a slight bilateral prominence of the medial retropharyngeal lymph nodes on the floor of the left and right medial compartments. Dental radiography was performed (right and left oblique, and dorsoventral) as well as thorax radiography and ultrasonography to detect metastasis: the results of all these examinations were negative.

A pathological examination of biopsied tissues belonging to the two pathological areas (base of tongue and epiglottis) revealed an exophytic lobular submucosal nodular lesion with a pushing border and “basaloid-like” architecture (Fig. 3). Neoplastic and perineoplastic tissues were colonized by a large amount of fungi, presenting endospore-forming sporangia of variable size (60–500 μ m) and stage of maturation (Fig. 3) with a central nucleus and a prominent nucleolus surrounded by basophilic granular material and a PAS-positive, GMS-negative unilamellar wall. On the basis of their morphology, these fungi were probably *Rhinosporidium* spp., as occasionally reported by other authors [3, 13]. The neoplastic cells were present in cribriform nests and sheets with a focal tubule formation, showing a cuboidal shape with large nuclei having small nucleoli and a clear chromatin pattern. Squamous differentiation and features of an adenoid cystic carcinoma were not identified. The malignant cells were positive for cytokeratin 7, but negative for cytokeratins 8/18, smooth

*CORRESPONDENCE TO: LAUS F., School of Veterinary Medical Sciences, University of Camerino, Via Circonvallazione 93–95, 62024, Matelica (MC) Italy. e-mail: fulvio.laus@unicam.it

©2014 The Japanese Society of Veterinary Science

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives (by-nc-nd) License <<http://creativecommons.org/licenses/by-nc-nd/3.0/>>.

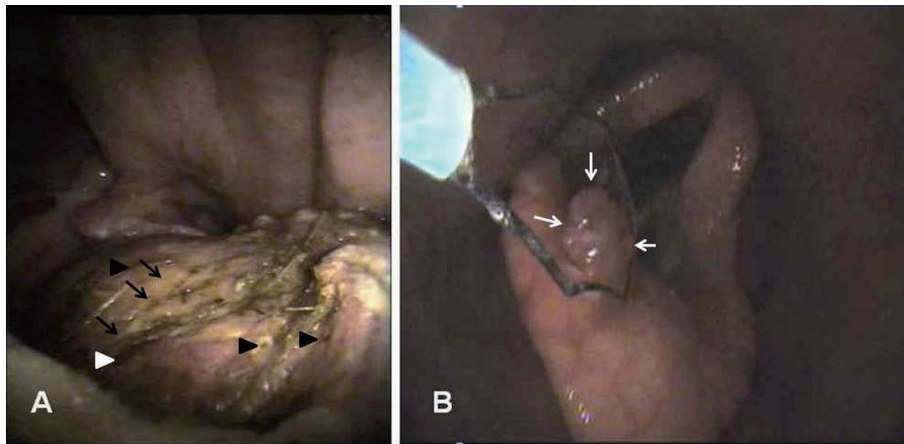


Fig. 1. Endoscopic appearance of the tumors. (A) Tongue: note the congestion, the granular appearance (arrows) and the small ulcerative areas (arrowheads) (B) Epiglottis: note the tissue protruding from the right dorsal aspect of the epiglottis (arrows).



Fig. 2. Ultrasonography of the tongue. Note the completely altered unilateral appearance with large hypoechoic areas (black arrows) surrounded by a small amount of heterogeneous tissue (white arrows). Lingual muscular tissue on the left side is ultrasonographically normal (NT) as is the tissue rostral to the lesion (not seen in the figure).

muscle actin and smooth muscle myosin (Fig. 4). The mass was diagnosed as adenocarcinoma of minor salivary gland origin located on the tongue base with a focal involvement of the epiglottis. The tongue biopsy revealed obvious positive margins.

A transendoscopic electrosurgery loop inserted in the right nasal cavity was used for surgical removal of the adenocarcinoma found on the epiglottis. At the same time, forceps passed through the work channel of an endoscope driven in the left nasal cavity were used to collect the removed tumors. A second histological examination was performed on this tissue, confirming the first diagnosis. The resected areas of the epiglottis showed margins that were negative

for malignancy.

Intralesional chemotherapy was not considered based on the owner's request, and treatment with flunixin meglumine, 1.1 mg/kg IV, SID, along with benzylpenicillin sodium, 16,000 U/kg IM, BID and streptomycin, 10 mg/kg IM, SID, was begun and continued for 15 days. The horse started to be fed gruel made from moistened pellets and flours several times per day and to eat a sufficient amount of food throughout the day. After two months, the clinical condition of the horse seemed to be stable.

Tumors involving the oral cavity of the horse are uncommon. The most frequent sites for oral neoplasia in the horse are the gingivae, dental alveoli and lips [6].

The tumors that can be found on the tongue are the rhabdomyosarcoma [4, 7], lymphosarcoma [14], mast cell tumor [17] and chondrosarcoma [22]. There is a report about an atypical perineurial proliferative disorder [21]. Oral SCC (squamous cell carcinoma) can involve the lips, the mucosa [5], the hard palate [11] and the tongue [5, 11]. Invasive SCCs, as well as fibrosarcomas, have a high recurrence rate after surgical excision [6]. Up to now, the most locally aggressive tumors of the oral cavity have been considered SCCs [19]. Also, spread of a primary neoplasm arising in the tongue to local draining lymph nodes has been described in a 10-year-old Shetland pony affected by a lymphosarcoma [14].

Because the mucosa of the base of the tongue contains the squamous epithelium, minor salivary glands and lymphoid tissue, the histology of malignant neoplasms that arise from this region of the oropharynx is quite varied and sometimes confusing.

In humans, most tongue cancers (more than 95%) are histologically characterized as squamous cell carcinoma; adenocarcinoma of the tongue, often arising from minor salivary glands, occurs in fewer than 2% of all tongue malignancies [18] and in 20% of all lingual minor salivary gland tumors [12, 20]. The disease process often affects adjacent

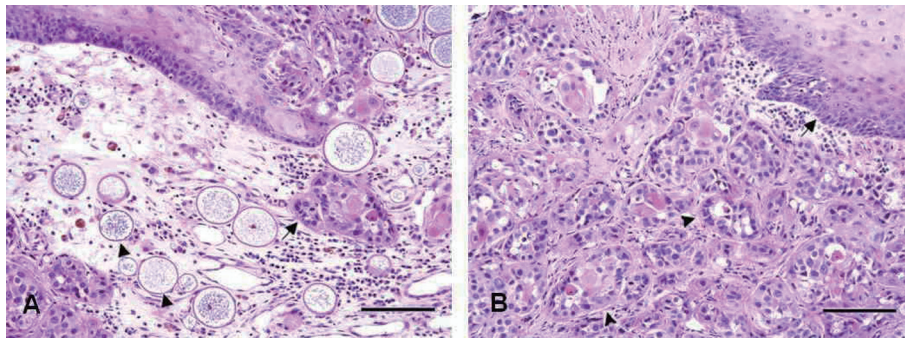


Fig. 3. Histology sections of the equine tongue- and epiglottis-associated adenocarcinoma not otherwise specified a being of minor salivary gland origin. (A) Medium-power photomicrograph of the epiglottis lesion, demonstrating its neoplastic infiltration in the submucosa (arrow), upon the epithelium, and contemporary colonization of fungi (arrowheads). (B) Tongue-associated primary tumor photomicrograph demonstrating arrangement of the neoplastic cells in cribriform nests, sheets (arrowheads) and focal tubules surrounded by severe inflammatory, subepithelial infiltration (arrow). (H&E; Bar=500 μ m).

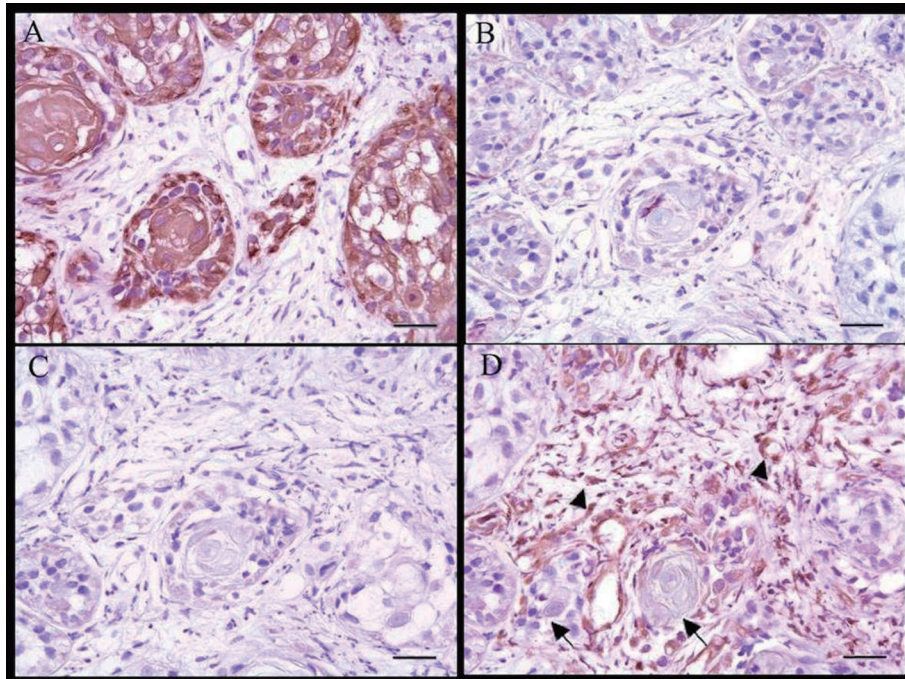


Fig. 4. Immunohistochemistry of the equine tongue-associated adenocarcinoma of minor salivary gland origin. (A) Strong immunostaining with cytokeratin 7 is only detected in the carcinomatous islands. (B) Immunostaining with cytokeratins 8/18 is almost totally negative. Only occasional and very scant cytoplasm positivity is detected. (C) The tumoral mass is totally negative for smooth muscle myosin. (D) Strong smooth muscle actin staining is observed only in the interstitial areas of the neoplastic tissue, in which scattered smooth muscle cells are present. The constant negativity of neoplastic epithelial cells (arrows), demonstrating no staining, is indicative of an absent myoepithelial cell component or differentiation. The noted area of positive staining (arrowheads) represents SMA uptake in arterial capillary wall. (IHC; Bar=200 μ m).

structures, primarily the larynx [18].

The involvement of the base of the tongue and pharynx can physically affect their function, leading to onset of progressive dysphagia [6], and it can sometimes be difficult

to understand from where lesion arose primarily [8]. Schuh [16] reported for the first time SCC of the tongue in 3 horses, and the clinical presentation was typical with an ulcerate surface and severe, superficial suppurative inflammation, which

is very similar to our report. The author reported that SCC of the tongue resulted in metastases in local and mediastinal lymph nodes and the lungs. In addition, metastatic behavior is rare in SCCs, especially in the oral form [9, 10], but can be possible for adenocarcinomas of salivary glands (parotid and submandibular glands) [5]. The adenocarcinoma reported in the present paper probably arose from a minor salivary gland of the tongue base, but did not seem to result in metastasis in the lungs when investigated by X-ray and ultrasonography. In any case, the slight enlargement of the retropharyngeal lymph nodes in the present case needs to be investigated, if possible, after the horse dies or after it is euthanized.

As reported by some authors [1, 15], risk factors for the development of base of tongue carcinoma are suggested to be nutritional deficiencies and infectious agents (especially papillomavirus and fungi). In this horse, no specific deficiency was found, and its papilloma virus infection status was unknown. On the other hand, a large fungal colonization of perineoplastic and neoplastic tissue was observed. Since the association between microorganisms and tumors in humans is well known and proven, the possible correlation in this case needs more investigation.

Generally, the prognosis for human cases of adenocarcinoma is more favorable than that for squamous cell carcinoma [2]. However, survival varies greatly depending on tumor stage, grade and treatment modalities used. On the basis of our review of the previous literature, the present case is the first report of equine adenocarcinoma arising from the minor salivary glands located on the dorsum of the tongue and involving the epiglottis with presence of fungal super infection.

Regarding the clinical behavior of the adenocarcinoma in the present case, it was very similar to that of an SCC, which can also strongly affect the ability to eat and is very aggressive and destructive for surrounding tissue [5, 16]. Horses with a tongue mass are generally presented to a veterinarian, because of weight loss, poor body condition and increasing difficulty in eating. In our case, the horse did not show difficulty in swallowing, and no nasal discharge containing food was present as found in other cases. The gelding was only not able to chewing normally and to drive the food towards the oropharynx and nasopharynx. After administration of anti-inflammatory drugs and antibiotic treatments, the situation got better, probably due to removal of the infective and edematous component of inflammation surrounding the neoplastic tissue. In the authors' opinion, adenocarcinomas should be included in the list of differential diagnoses for oral disorder causing chewing alteration in horses, especially in geriatric equine patients, and based on its clinical appearance, the principal distinction should be made with SCC.

REFERENCES

1. Attner, P., Du, J., Näsman, A., Hammarstedt, L., Ramqvist, T., Lindholm, J., Marklund, L., Dalianis, T. and Munck-Wikland, E. 2011. Human papillomavirus and survival in patients with base of tongue cancer. *Int. J. Cancer* **128**: 2892–2897. [Medline] [CrossRef]
2. Biller, H. F., Lawson, W. and Baek, S. M. 1983. Total glossectomy. A technique of reconstruction eliminating laryngectomy. *Arch. Otolaryngol.* **109**: 69–73. [Medline] [CrossRef]
3. Burgess, H. J., Lockerbie, B. P., Czerwinski, S. and Scott, M. 2012. Equine laryngeal rhinosporidiosis in western Canada. *J. Vet. Diagn. Invest.* **24**: 777–780. [Medline] [CrossRef]
4. Castleman, W. L., Toplon, D. E., Clark, C. K., Heskett, T. W., Farina, L. L., Lynch, T. M., Bryant, U. K., Del Piero, F., Murphy, B. and Edwards, J. F. 2011. Rhabdomyosarcoma in 8 horses. *Vet. Pathol.* **48**: 1144–1150. [Medline] [CrossRef]
5. Easley, J., Dixon, P. M. and Schumacher, J. 2011. *Equine Dentistry*. 3rd ed., Elsevier Limited, London.
6. Gerard, M. P. 2009. Oral cavity masses. pp 348–350. In: *Current Therapy in Equine Medicine*, 6th ed. (Robinson N. E. and Sprayberry K.A. eds.), Saunders, St. Louis, Missouri.
7. Hanson, P. D., Frisbie, D. D., Dubielzig, R. R. and Markel, M. D. 1993. Rhabdomyosarcoma of the tongue in a horse. *J. Am. Vet. Med. Assoc.* **202**: 1281–1284. [Medline]
8. Howie, F., Munroe, G., Thompson, H. and Murphy, D. 1992. Palatine squamous cell carcinoma involving the maxillary sinus in two horses. *Equine Vet. Edu.* **4**: 3–7. [CrossRef]
9. Johnson, P. J. 1998. Dermatologic tumors excluding sarcoids. *Vet. Clin. North Am. Equine Pract.* **14**: 625–658. [Medline]
10. Jubb, K. V. F., Kennedy, P. C. and Palmer, N. 1993. *Pathology of Domestic Animals*, Vol. 2, 4th ed., Academic Press, New York.
11. Knottenbelt, D. C. and Pascoe, R. R. 1994. *Diseases and Disorders of the Horse*. Wolfe, London.
12. Lim, J. H., Lim, J. Y., Kim, Y. M., Kim, C. S., Choi, S. J., Yi, H. G., Choi, W. G. and Lee, M. H. 2012. Primary diffuse large B cell lymphoma of the base of tongue. *J. Cancer Res. Ther.* **8**: 135–137. [Medline] [CrossRef]
13. Nollet, H., Vercauteren, G., Martens, A., Vanschandevijl, K., Schauvliege, S., Gasthuys, F., Ducatelle, R. and Deprez, P. 2008. Laryngeal rhinosporidiosis in a Belgian warmblood horse. *Zoonoses Public Health* **55**: 274–278. [Medline] [CrossRef]
14. Rhind, S. M. and Dixon, P. M. 1999. T cell-rich B cell lymphosarcoma in the tongue of a horse. *Vet. Rec.* **145**: 554–555. [Medline] [CrossRef]
15. Rischin, D. 2010. Oropharyngeal cancer, human papilloma virus, and clinical trials. *J. Clin. Oncol.* **28**: 1–3. [Medline] [CrossRef]
16. Schuh, J. C. L. 1986. Squamous cell carcinoma of the oral, pharyngeal and nasal mucosa in the horse. *Vet. Pathol.* **23**: 205–207. [Medline] [CrossRef]
17. Seeliger, F., Hess, O., Pröpsting, M. J., Naim, H. Y., Kleinschmidt, S., Woehrmann, T., Germann, P. G. and Baumgärtner, W. 2007. Confocal laser scanning analysis of an equine oral mast cell tumor with atypical expression of tyrosine kinase receptor C-KIT. *Vet. Pathol.* **44**: 225–228. [Medline] [CrossRef]
18. Seikaly, H., Rieger, J., Wolfaardt, J., Moysa, G., Harris, J. and Jha, N. 2003. Functional outcomes after primary oropharyngeal cancer resection and reconstruction with the radial forearm free flap. *Laryngoscope* **113**: 897–904. [Medline] [CrossRef]
19. Straffuss, A. C. 1976. Squamous cell carcinoma in horses. *J. Am. Vet. Med. Assoc.* **168**: 61–62. [Medline]
20. Tseng, W. C., Chang, S. Y., Chu, P. Y., Tai, S. K., Wang, Y. F., Shiao, A. S. and Tsai, T. L. 2011. Management of base of tongue squamous cell carcinoma: experience with 85 patients in Taipei Veterans General Hospital. *J. Chin. Med. Assoc.* **74**: 220–225. [Medline] [CrossRef]
21. Vashisht, K., Rock, R. W. and Summers, B. A. 2007. Multiple masses in a horse's tongue resulting from an atypical perineurial cell proliferative disorder. *Vet. Pathol.* **44**: 398–402. [Medline] [CrossRef]
22. Wilson, G. J. and Anthony, N. D. 2007. Chondrosarcoma of the tongue of a horse. *Aust. Vet. J.* **85**: 163–165. [Medline] [CrossRef]