BJVP
Brazilian Journal of Veterinary Pathology
ISSN 1983-0246

Case report

Ossifying Oronasal Carcinoma in a Horse

Ana Patrícia de Carvalho da Silva[1], Fabiane Cassou[1], Bruno Santos Cândido Andrade[1], Luiz Carlos Vargas de Oliveira Ramos[1], Tatiane Alves da Paixão[2], Geraldo Eleno Silveira Alves[1], Renato Lima Santos[1]*

[1]Departamento de Clínica e Cirurgia Veterinárias, Escola de Veterinária, Universidade Federal de Minas Gerais, Brasil.
[2]Departamento de Patologia Geral, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Brasil.

*** Corresponding Author:** Departamento de Clínica e Cirurgia Veterinária, Escola de Veterinária, Universidade Federal de Minas Gerais, Av. Presidente Antônio Carlos, 6627 – CEP 30161-970, Belo Horizonte, MG, Brazil. Phone: 55-31-3409-2239; Fax: 55-31-3409-2230; E-mail: rsantos@vet.ufmg.br

Submitted September 29th 2012, Accepted October 21st 2012

Abstract

Oral and nasal carcinomas are common in domestic animals, but osseous neoformation in epithelial tumors is rare. This is the first case of an ossifying carcinoma described in horse. This report describes a case of oronasal ossifying carcinoma in a 5-year-old Quarter Horse stallion that developed swelling on the right side of the face. Grossly, there was a neoplastic mass that occupied the entire right nasal cavity and extended into the oral cavity. Histologically, there was neoplastic proliferation of epithelial cells, which were arranged in cords and nests supported by an abundant fibrovascular stroma with osteoid deposition and osseous differentiation in the stroma with abundant osteoclast-like cells. Immunohistochemistry demonstrated immunopositivity for cytokeratin in epithelial cells and immunopositivity for vimentin in stromal cells including the osteoclast-like cells. Immunohistochemical findings favored a diagnosis of ossifying oronasal carcinoma.

Key Words: equine, tumor, neoplasia, oral, nasal.

Introduction

Sinonasal tumors are uncommon in horses, they can originate at the oral, nasal or sinusal cavities, and often respond poorly to treatment (12). Occasionally these tumors may expand into the orbit or the brain (13, 23).

Incidence of neoplasms as well as its risk factors varies among domestic animals (34). For instance, the most common neoplasm that affects the nasal and paranasal regions in horses is the squamous cell carcinoma (12). In contrast to other domestic animal species, primary neoplasia of the oral cavity is rare in horses, but when present, it may have origin from bone, teeth or epithelial tissues (21). Carcinomas are relatively common in the oral and nasal cavities of domestic animal species, including adenocarcinoma, transitional carcinoma, squamous cell carcinoma, and adenosquamous carcinoma, whereas odontogenic tumors include ameloblastoma, keratinizing ameloblastoma, acantomatous ameloblastoma, cementoma, and ameloblastic fibro-odontoma (11, 33).

Malignant tumors of the paranasal sinuses are also rare in humans (4), but the squamous cell carcinoma is the most common, followed by lymphoma, adenocarcinoma, melanoma, and salivary gland tumors (10). A few cases of carcinoma with a sarcomatous component, carcinosarcomas, or heterotopic ossification have been reported in humans (22, 26).

Osseous neoformation in epithelial tumors is rare in domestic animal species, and there are no previous reports of ossifying carcinomas in domestic animal species. Here we report an ossifying oronasal carcinoma in a horse.

Case description

A five year old Quarter Horse stallion was presented to the Veterinary Hospital of the Universidade Federal de Minas Gerais with a history of impaired athletic performance, right unilateral facial swelling, and nasal purulent secretion (Figure 1A/B). Clinical and radiological examinations demonstrated changes in the right maxillary and frontal sinuses, with involvement of the periodontal structures of the 107, 108, and 109 teeth, with increased mobility of the first two. Considering the clinical finding of dental changes upon oral inspection, radiographs were taken at an oblique position prioritizing imaging of the dental arcade. In addition, a decreased radiolucency of the maxillary sinus was observed, which was compatible with the nasal discharge suggestive of sinusitis. There was also abnormal sonority upon digital percussion in the area of facial swelling. The 107 and 108 teeth were easily extracted. Alveolar cavities were flushed with 2% chlorhexidine followed by occlusion of the alveolar cavities with a cotton ball to prevent accumulation of food material. This procedure was repeated daily until cicatrization. Systemic treatment was based on the association of penicillin (22,000 IU), gentamicin (2.2 mg), and metronidazole (10 mg/Kg) for 15 days, and flunixin meglumine (1.1 mg/kg) for 10 days.

The original clinical diagnostic hypothesis included periodontal disease associated with sinusitis. Neoplasia was suspected due to the gross appearance of the tissue adhered to the 108 tooth (Figure 1C), which was sampled for histological processing. Tissue samples were fixed by immersion in 10% buffered formalin, processed for paraffin embedding, and 5 µm-thick sections were stained with hematoxylin and eosin and immunohistochemistry for labeling of cytokeratin (clone AE1AE3 - Dako, code M3515, dilution 1:100) and vimentin (clone Vim3B4 (Dako, code M7020, dilution 1:100). Immunohistochemistry was performed by incubating with the primary antibody for 30 minutes, followed by incubation with the secondary antibody after washing in PBS, and then with streptavidin-biotin-peroxidase for 20 minutes, using a commercial kit (LSAB+ kit; Dako Corporation, Carpinteria, CA) according to the manufacturer's instructions. Reaction was revealed with 0.024% diaminobenzidine (DAB; Sigma), and sections were counterstained with Mayer's hematoxylin.

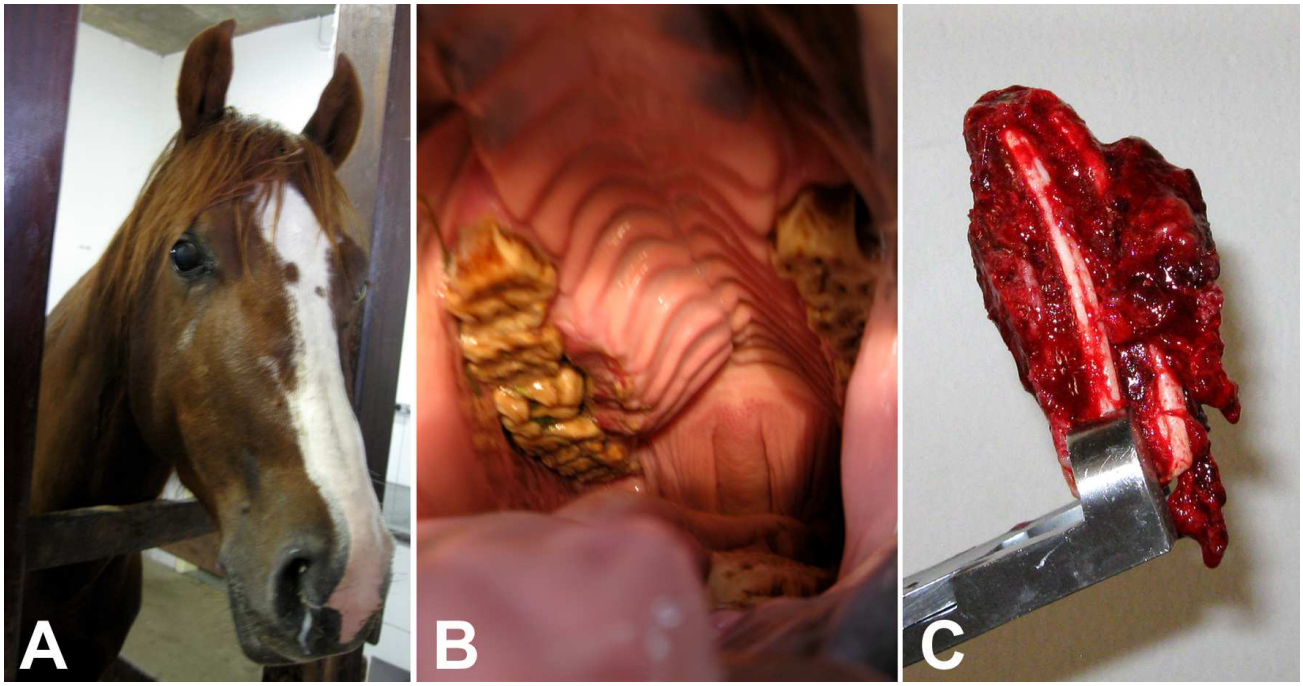

Figure 1. Clinical and surgical features of an oronasal ossifying carcinoma in a horse. (A) Swelling of the right side of the face with purulent nasal secretion. (B) Deformation of the hard palate with ulcerative periodontitis of the 107, 108, and 109 teeth. (C) Extracted 108 tooth with a tissue mass adhered to the periodontum.

After maceration, the tissue adhered to 108 tooth had a spiculated and arborescent appearence with a gross appearance that resembled a coral (Figure 2A). Based on these findings, a cementoma was considered for the differential diagnosis.

The owner elected to pursue clinical treatment at the farm until ninety days later, when the horse was once

again admitted at the Veterinary Hospital due to progressive weight loss, and respiratory distress. Upon second admission, the horse presented with a facial swelling adjacent to the right maxillary and nasal bones, and cachexia, inappetence, apathy, and respiratory distress due to a complete obstruction of the right nasal cavity. Due to poor prognosis euthanasia was elected.

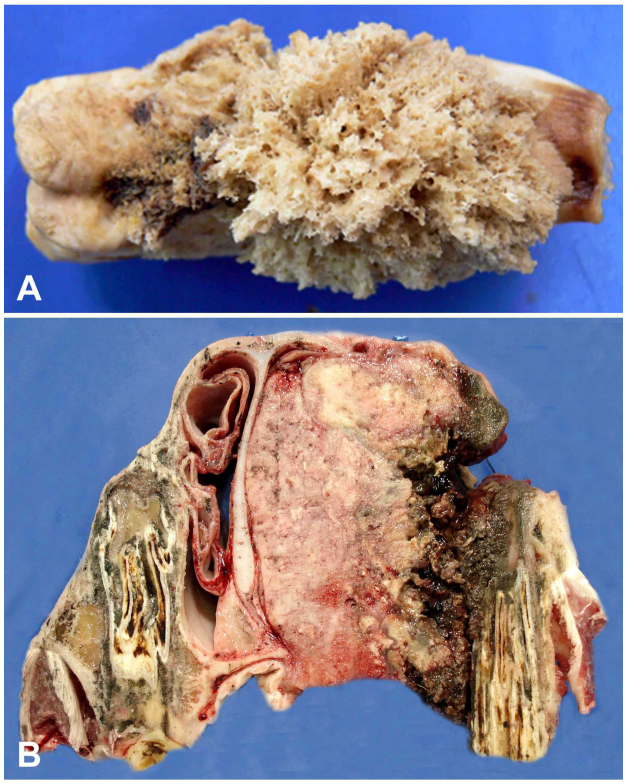

Figure 2. Gross appearance of an oronasal ossifying carcinoma in a horse. (A) Macerated 108 tooth with spiculated mineralized exophytic proliferation resembling a coral. (B) Whitish-yellow neoplastic mass completely obstructing the right nasal cavity, with deviation of the nasal septum and compression of the left nasal cavity.

At necropsy, transverse sections of the nasal and maxillary bones revealed a neoplastic mass with approximately 30x4x8 cm. The neoplastic tissue was invasive, whitish-yellow, ulcerated, moderately vascularized, firm, and on the cut surface there was a multilobulated appearance with lobules separated by septa of dense connective tissue with multifocal mineralization (Figure 2B). The neoplastic mass invaded rostrally and laterally the nasal and maxillary bones, reaching the alveolar bone, teeth, and hard palate. Microscopically, the neoplastic tissue was composed of epithelial neoplastic proliferation, non encapsulated, poorly demarcated, infiltrative, with cells arranged in cords and nests, supported by a stroma ranging from thin fibrovascular septa to dense bands of connective tissue. In some areas, stromal cells had a stellate morphology. In some areas of the stroma, there was deposition of osteoid matrix poorly to moderately mineralized (arrow), associated with multinucleated cells similar to osteoclasts (Figure 3A). There was mineralized matrix with lacunas containing osteocyte-like cells, compatible with mineralized osseous tissue.

Neoplastic epithelial cells had abundant well demarcated cytoplasm, with intercellular bridges, and centrally located nucleus with sparse chromatin (Figure 3B). Cells located in the periphery of cords and nests had a more elongated or columnar shape. Mitotic index ranged from one to seven mitotic figures per high magnification microscopic field. There were multifocal extensive areas of necrosis and hemorrhage.

Immunohistochemistry demonstrated that epithelial neoplastic cells were strongly positive for cytokeratin (Figure 3C), whereas stromal cells were strongly vimentin positive (Figure 3D). In addition, selected samples in this case were submitted for consultation at the Armed Forces Institute of Pathology (AFIP). Their immunohistochemical pannel included cytokeratins (AE1/AE3, AE5/AE6 and 19), vimentin, p63, and nuclear protein in testis (NUT). Neoplastic cells were strongly positive for cytokeratins (clones AE1/AE3 and AE5/AE6), and negative for the other markers. Based on their immunohistochemical panel, AFIP proposed the diagnosis of squamous cell carcinoma, in spite of the absence of squamous differentiation.

This case illustrates the need for a thorough differential diagnosis in cases of oronasal and sinusal diseases in horses. Most diseases affecting the nasal cavity have similar clinical signs including such as epistaxis, dyspnea, and nasal secretion (18). Therefore, biopsy and histopathological evaluation is a powerful tool in most cases for establishing a final diagnosis (2, 19, 28, 29, 32).

Although the hypothesis of preexisting osseous tissue should be considered, histological features clearly indicated neoformation of osseous tissue with abundant non mineralized or poorly mineralized osteoid matrix.

Several human tumors have been associated with osseous metaplasia including basal cell carcinoma (7, 3, 14, 27, 30), atypical fibroxanthoma (5), melanocytic nevus (6, 17), melanoma (9, 20) pilomatricoma (16), trichofolliculoma (24), hemangioendothelioma, among others (15). Heterotopic ossification may originate from osteoprogenitor stem cells that start producing osteoid matrix upon stimulation (31).

Odontogenic tumors have also been considered for the differential diagnosis. The gross findings suggested a possible cementoma, which is a mesenquimal odontogenic tumor characterized by the deposition of cemental matrix around the tooth that usually invades and leads to destruction of the alveolar bone (1, 8, 25). However, microscopic morphology did not support this diagnostic hypothesis. Furthermore, AFIP consultation indicated that the neoplastic cells were negative for cytokeratin 19 that is often expressed in other odontogenic tumors.

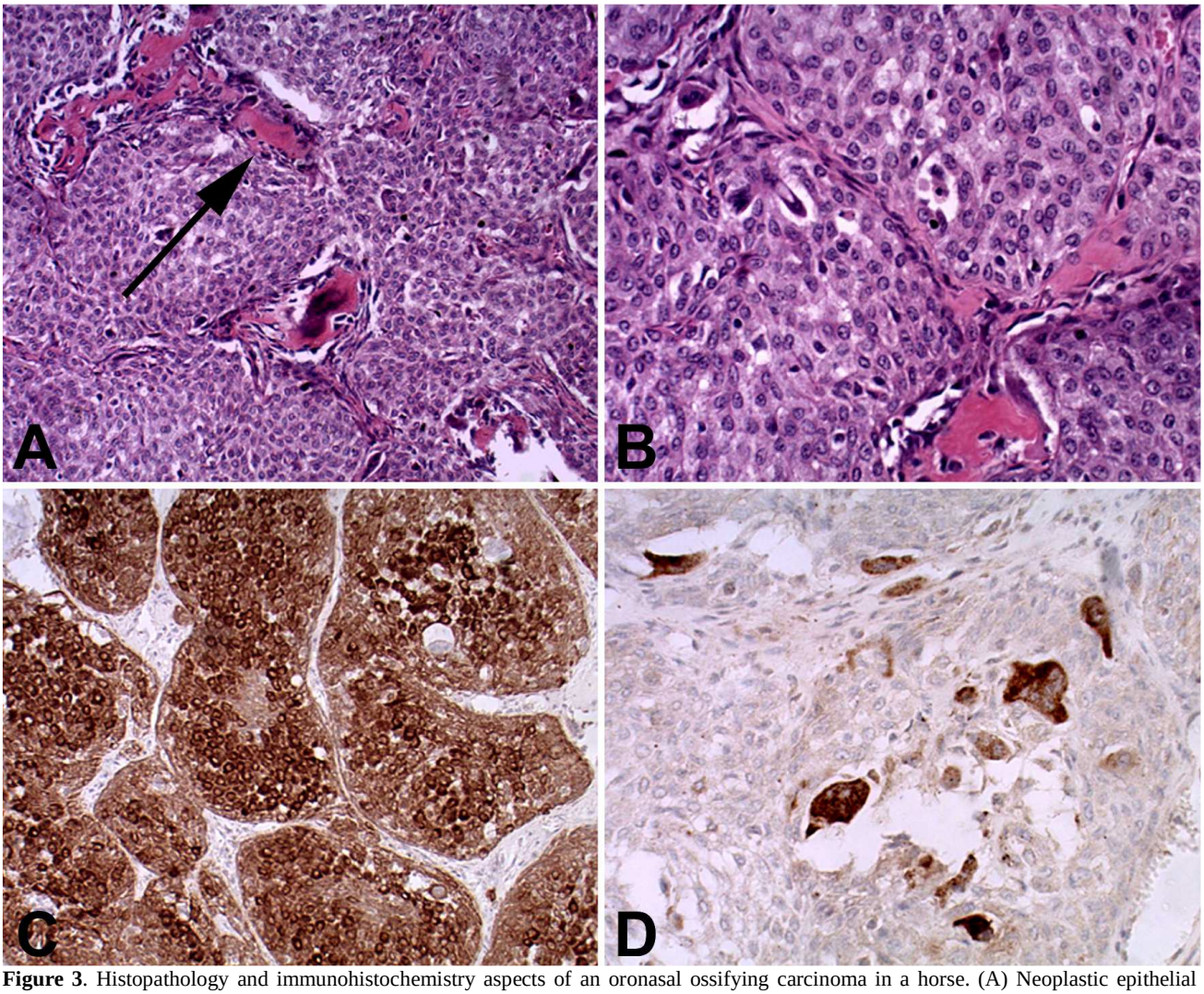

Figure 3. Histopathology and immunohistochemistry aspects of an oronasal ossifying carcinoma in a horse. (A) Neoplastic epithelial cells arranged in lobules with multifocal osseous mineralized tissue (arrow), HE, 10x objective (B) Neoplastic epithelial cells sustained by a dense fibrovascular stroma, HE, 20xobjective (C) Neoplastic cells strongly positive for cytokeratin, Streptavidin-biotin-peroxidade, 10x objective (D) Stromal multinucleated osteoclast-like cells strongly immunostained for vimentin, Streptavidin-biotin-peroxidade, 20x objective.

In conclusion, no oral or nasal carcinomas associated with ossification of the stroma have been previously reported in horses. Based on the pathological and immunohistochemical findings, and the complete lack of classification compatible with this tumor, a diagnosis of ossifying oronasal carcinoma was established.

Acknowledgments

This study was supported by CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico, Brasília, Brazil) and FAPEMIG (Fundação de Amparo a Pesquisa do Estado de Minas Gerais, Belo Horizonte, Brazil). We thank the Armed Forces Institute of Pathology for providing consultation in this case.

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