Case Report

Mandibular squamous cell carcinoma in a young horse

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Summary

Squamous cell carcinoma (SCC) is a frequently reported neoplasm in the horse. However, oral forms are uncommon and represent only 7% of all SCC. A literature review reveals a total of 13 cases of oral SCC with no apparent sex or breed predisposition but predominantly adult and old horses, mean age 16.5 years. This case report describes a 3.5-year-old pony filly that was presented for investigation of a mandibular fistula of 3 weeks’ duration. The clinical and histopathological findings of mandibular squamous cell carcinoma in this filly are described in detail.

Introduction

Oral squamous cell carcinoma (SCC) is a malignant neoplasm of stratified squamous epithelium. These tumours are characteristically slow growing but they can be very destructive. Metastases to local lymph nodes may occur. It usually appears in adult horses and may involve the lips, hard palate, tongue or oral mucosa and quite commonly invades the nasal cavity and the paranasal sinuses (Leyland and Baker 1975).

The following Case Report describes the difficulties that can arise making an accurate ante mortem diagnosis of a mandibular carcinoma in a young horse. The literature on previously reported squamous cell carcinomas in the horse is also reviewed.

Case history

A 3.5-year-old pony filly was presented to the equine clinic of the Veterinary School, University of Lyon, with a 1.5 month history of a fistula in the rostral aspect of the mandible. The owner initially described a 2 cm diameter gum wound rostrally to 301 and 401 incisors. Local treatment was performed on a daily basis and loss of a bone fragment was reported. The referring veterinarian had performed curettage 3 weeks prior to presentation, with removal of several bony fragments. The filly received antibiotics for 5 days with no evident improvement. Following that, the filly developed an exuberant granulation tissue mass, with dysphagia, halitosis and ulceration of this mass.

Clinical findings

Ante mortem diagnosis

On presentation to the hospital, physical examination indicated normal body temperature, pulse and respiratory rate. A complete blood count and chemistry panel were found to be within normal limits. The right mandibular lymph node was increased in size but was not painful on palpation. The granulation tissue was heterogenic, necrotic, had a fetid odour and the mass separated the first left (Triadan 301) and right (Triadan 401) mandibular incisors (Fig 1a). There was a prognathism of the mandible in part due to the exuberant granulation tissue (Fig 1b). A fistula was seen in the ventral part of the lower lip.

Radiographic studies demonstrated a multilocular soft tissue mass cranial to a radiolucent zone close to the incisor teeth (Fig 2a). The incisors 301 and 401 were displaced with loss of normal alveolar bone (Fig 2b).

Under sedation and regional anaesthesia the mass was debrided and bony fragments removed. Several fragments of abnormal tissue were obtained during debridement. Samples were fixed in 10% formalin and embedded in paraffin, sectioned at 5 µm, and stained with haematoxylin and eosin. Tumour samples for histopathology revealed extensive epithelial proliferation of the mucosa composed of numerous islands of epithelial cells separated by moderate quantities of dense fibrovascular stroma. Neoplastic cells were cuboidal to polygonal, with abundant eosinophilic cytoplasm, distinct cell borders and very rare intercellular bridges. A small number of cells at the centre of the islands had hypereosinophilic cytoplasm and a hyperchromatic condensed nucleus (keratinisation). The rest of the nuclei had a hyperchromatic nucleus.
were round, central, with finely stippled chromatin and 1–3 prominent magenta nucleoli. Mitotic figures were few and anisocytosis and anisocaryosis were marked. Cellular atypia such as canyomegaly, cytomegaly and multinucleation were frequently noted. The overlying mucosa was extensively ulcerated and the exposed submucosa contained large numbers of neutrophils with fewer lymphocytes, plasma cells and macrophages admixed, also found in the sublingual skeletal muscle (Fig 3b). The morphological diagnosis was a poorly differentiated gingival carcinoma and the primary differential was a squamous cell origin based on the very rare intercellular bridges.

A mandibulectomy was suggested to the owners but euthanasia was elected for economic reasons and because of the guarded prognosis associated with squamous cell carcinoma.

**Post mortem diagnosis**

At necropsy, there was no evidence of tumour metastasis to the lung or other organs. Macroscopically the mass measured 10 cm in length, was hard and strongly adherent to the mandibular bone (Fig 4a). A transverse section of the mandibular symphysis revealed a 10 x 4 cm cavity around the roots of the first incisors created by the surgical debridement (Fig 4b). The right sub-mandibular lymph node measured 14 cm in length compared to 9 cm for the left one (Fig 5). Samples for histopathology were obtained from the right lymph node. Sections revealed marked lymphoid hyperplasia and drainage of suppurative inflammation with no evidence of metastases.

**Discussion**

Squamous cell carcinoma is a frequently reported neoplasm in the horse (Dorn and Priester 1976). It most frequently involves male genitalia, ocular and periorcular tissues, female genitalia (Strafuss 1976), and the stomach (Strafuss 1976; Sundberg 1977). Less frequent locations include the oesophagus (Roberts and Kelly 1979), skin, hard palate (Leyland and Baker 1975; Knottenbelt and Pascoe 1994), arytenoid cartilage, gullet pouch (Moulton 1978), maxillary sinus, perineal tissues, peritoneal cavity, maxilla, lymph nodes (Sundberg et al. 1977) and nasal cavity (Leyland and Baker 1975; Traver et al. 1977).

Squamous cell carcinomas arising from the mucosa of the oral, pharyngeal and nasal cavities were first described by Randall et al. (1984). Oral SCC represents 7% of all SCC in horses (Orsini et al. 1991) and it is often suggested that the primary tumour develops in the paranasal sinuses or cavity and the destructive tissue involves the hard palate (Howie 1992). Oral SCC may also appear in chronically irritated hyperplastic alveolar epithelium in cases of chronic periodontitis (Knottenbelt and Kelly 2005).

A review of the literature found 13 cases of oral SCC (Randall et al. 1984; Schuch 1986; Orsini et al. 1991; Knottenbelt and Pascoe 1994; Faragalla 2002), which include tumours of the tongue, the lips, oral mucosa or rostral maxilla and mandible (Table 1). Analysis of the data indicates that equine oral SCC is most commonly found in adult and old horses, aged 8–27 years with a mean of 16.5 years. No sex or breed predisposition is apparent although correlation with nonpigmented skin and high levels of ultraviolet light have been discussed (Knottenbelt and Kelly 2005). To our knowledge there are no reports of SCC in horses aged <8 years. Our case report shows, however, that SCC can not rule out as a differential diagnosis of mandibular tumours.

Squamous cell carcinoma is a slow growing, usually destructive and ulcerative tumour. It can infiltrate widely into surrounding tissues of the mouth including the lips, oral mucosa, hard palate and tongue. Metastases to lymph nodes can occur and in theory tumour emboli can disseminate to the lungs and elsewhere, but the latter event is rare in oral forms. Depending on the location these tumours are often detected late. Large invasive tumours of the gum present as ulcerated and bleedin

| Table 1: Summary of 13 previously published cases of equine oral squamous cell carcinoma |
|-----------------------------------------------|--------------------------|------------------|----------------|
| Reference                                    | Age, gender and breed    | Tumour location  | Treatment               |
| Randall et al. (1984)                        | 5 cases: Male (mean 14 years; range 8–20 years), Female (mean 16 years; range 14–18 years); Appaloosa, Clydesdale, Quarter Horse, Standardbred | Maxillary gingiva, mandible, lower lip, buccal mucosa, oral mucosa | Euthanasia |
| Schuch (1986)                                | Adult Appaloosa female 22 years, Morgan gelding | Oral mucosa | Euthanasia |
| Schuch (1986)                                | Adult Morgan female 10 years, Mixed breed female | Tongue | Euthanasia |
| Orsini et al. (1991)                         | 13 years, Appaloosa male 27 years, Arabian male | Labial, gingival, last molar; Rostral aspect of maxilla | Euthanasia |
| Knottenbelt and Pascoe (1994)                 | 23 years, pony gelding | Lips | Cisplatin and 5-fluoracil (not effective) |
| Faragalla (2002)                             | 17 years, Tennessee Walker pregnant female | Buccal aspect of right mandible | Tooth extraction, euthanasia after C-section |
masses. When the tumour incorporates tooth roots, teeth may become dislodged and in almost all cases there is a fetid odour from the mouth.

Diagnosis of mandibular tumours can sometimes be difficult, usually because of concurrent longstanding infection or granulation tissue proliferation. The differential diagnosis includes other proliferative and invasive lesions of the soft tissues such as equine sarcoid, ossifying fibroma, haemangiosarcoma, myxomatous tumours, salivary adenocarcinoma and basal cell carcinoma. In our case given the age of the animal and the location of the tumour, an ossifying fibroma was suspected. These tumours are frequent in young animals (2 months–2 years), are considered to have a benign behaviour and have a fair to good prognosis. Initial debridement was performed in order to improve the animal’s comfort but also to obtain good histological samples. The diagnosis by biopsy can be misleading if the sample contains only stroma and inflammatory cells (Knottenbelt and Kelly 2005).

Radiography can help identify mass extension but appearance is variable. In this case we found a soft tissue mass with dislodgement of the incisor teeth, bone proliferation and loss of alveolar bone. Pulmonary radiographs were not performed because of the absence of clinical and haematological findings but should be recommended if surgical treatment is planned.

The microscopic appearance of the tumours varies considerably from well differentiated neoplasms composed of islands and nests of keratinised squamous epithelium with formation of keratin pearls to poorly differentiated tumours with little evidence of keratinisation, as seen in our case. Prominent desmoplastic stroma with marked inflammation is usually present.

Masses can be removed by surgery but may be associated with cosmetic and functional problems. Successful rostral surgical excision has been reported in a horse that survived for 5 months (Orsini et al. 1991). However, in that case, histopathological examination of tumour margins revealed neoplastic cells and the horse died during anaesthesia for adjunctive radiotherapy treatment (Orsini et al. 1991). In horses, rostral mandibulectomy was described by Richardson et al. (1991) in 5 cases of mandibular tumours, 3 of which were ossifying fibromas, as a simple and efficient treatment option with no complications and no recurrence of tumour. The cosmetic effect was mild and there was no noticeable functional impairment. No reports of mandibulectomy in carcinoma cases were found. In dogs, oral tumours involving the mandible are relatively common (Vernon and Helphrey 1983; Withrow and

Figure 1: Cranial a) and lateral b) views of the rostral mandibular mass in the 3.5-year-old filly.

Figure 2: a) Latero-medial and b) Dorso-ventral intraoral radiographs taken at the time of presentation.

Figure 3: a) Extensive obliteration of the mandibular bone by sheets and nests of tumour cells (decalcified section stained with haematoxylin and eosin, x20). b) Closer view of the sheets of poorly differentiated neoplastic epithelial cells showing little to no keratinisation (decalcified section stained with haematoxylin and eosin, x200).
SCC are reported in 16–27% of oral tumours in dogs (Bradley et al. 1984; Kosovsky et al. 1991) and as the most common oral tumour in the cat in which they represent 83% (Bradley et al. 1984). Mandibulectomy has resulted in satisfactory outcome in 77% (46/60) of dogs and cats (Vernon and Helphrey 1983). Outcome of mandibulectomy in cases of SCC in dogs was found to have a disease-free interval of 26 months (range 6–84 months) with 91% one-year survival rate.

Gamma radiation has been successful in the treatment of many oral tumours, although treatment is generally long term and possibly more expensive than surgery (Richardson et al. 1991). Iridium-192 interstitial brachytherapy using linear platinum-sheathed wires has been used to good effect (D.C. Knottenbelt, unpublished data) but this treatment carries human health risks, and is limited by the size and location of the mass. Some SCC respond to cisplatin and 5-fluorouracil application has been shown to resolve and improve some cases of SCC, especially small, ulcerated, and oral and lip lesions when combined with other therapies (Paterson 1997).

Clinical prognosis is generally poor but horses can survive several months to several years even with large masses. Complications include facial and oral distortion and loosening of teeth. Oral SCC is an invasive tumour but does not tend to metastasise beyond the regional lymph nodes, except in poorly differentiated tumours and with delayed surgical excision.

Although several individual reports have been published, a clinical retrospective study should be performed in order to obtain further information about treatment and outcome of SCC in horses.

References


Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

For treatment of gastric ulcers, **Dosage Regimen**

- To deliver dose to a 1250 lb (568 kg) horse at the rate of 1.8 mg omeprazole/lb body weight (4 mg/kg).

**Paste at the treatment dose rate of 1.8 mg omeprazole/lb body weight** (4 mg/kg), set the syringe plunger to the nearest the barrel is at the appropriate notch. Rotate the plunger ring 1/4 turn to lock it in place and ensure it is engaged. Failure to perform this step may result in part of the dose being lost or rejected. If any of the dose is lost, redosing is recommended.

**Pharmacokinetics:** In a pharmacokinetic study involving thirteen healthy, mixed breed horses (8 female, 5 male) receiving multiple doses of GASTROGARD Paste, administered to provide omeprazole at 1.8 mg/lb (4 mg/kg) daily for 28 days, no adverse reactions were observed.

**Pharmacodynamics:** In a study of pharmacodynamic effects using horses with gastric cannulae, secretion of gastric acid was inhibited in horses after omeprazole therapy. The safety of GASTROGARD Paste was evaluated in a chronic toxicology study in horses, which included evaluations of hematology, clinical chemistry, organ weights, body weight, and food consumption. No treatment related adverse effects were observed.

**Reproductive Safety:** Reproduction studies have revealed no adverse effect on reproduction in mice, rats, and rabbits. In the clinical trials, the use of GASTROGARD Paste in horses was not associated with adverse effects on reproduction (i.e., fertility, parturition, pregnancy outcome, or foal viability).

**Gastrointestinal Ulcers:** Gastric ulcers may recur in horses if therapy to prevent recurrence is not administered after the initial treatment is completed. Use GASTROGARD Paste in all cases to prevent recurrence of gastric ulcers.

**Non-steroidal and steroidal anti-inflammatory agents, diuretics, tranquilizers and vaccines.**

**Clinical signs in foals may include: bruxism (grinding of teeth), excessive salivation, colic, cranial nerve disturbances.** In foals and horses, inappetence or decreased appetite, recurrent colic, intermittent loose stools or chronic diarrhea, poor hair coat, poor body condition, or poor growth performance. Clinical signs may also include fever, anemia, weight loss, and degenerative joint disease.

**Non-invasive diagnosis of growths in the equine nasal passage.**


**Vet. Surg.** 12, 26-29.

**Vet. Pathol.** 23, 150-152.


**J. Am. vet. med. Ass.** 199, 1179-1182.

**J. Am. vet. med. Ass.** 168, 62-64.


**J. Am. vet. med. Ass.** 150, 150-152.

**Pharmacology:** The garlic is used in treating canine and feline cutaneous disorders due to their antifungal properties. Dosage should be administered on a daily basis. A single dose of the garlic is recommended to be administered at a rate of 1.8 mg omeprazole/lb body weight once daily for fifteen days.

**Gastroscopic examination of the stomach is recommended at the end of the study, or in case of clinical indications.**

**Pastoral Care of Horses:** Paste should be administered orally once-a-day for 4 weeks at the recommended dosage of 1.8 mg/lb body weight. The stomach was examined at the end of the study, or in case of clinical indications.

**Clinical symptoms:** The garlic is used in treating canine and feline cutaneous disorders due to their antifungal properties. The garlic is used in treating canine and feline cutaneous disorders due to their antifungal properties.