

FORMALIN USE FOR SURGICAL MARGIN CONTROL AFTER RESECTION OF GINGIVAL FIBROMA IN A MARE

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Summary

Gingival fibroma is rare in horses and is most commonly located in the rostral portion of the maxilla or mandible; however, more caudal locations have occasionally been reported. Although these lesions are benign, they have a high recurrence rate if all abnormal tissue is not completely removed. Standard treatment typically involves surgical excision, sometimes combined with adjunctive chemotherapy. In certain cases, more aggressive procedures such as mandibulectomy may be required depending on tumour size and anatomical location. However, these approaches are not always feasible due to anatomical constraints or financial limitations. This report describes the management of a gingival fibroma in a horse in which complete surgical excision was not possible. Following tumour recurrence after initial surgical debulking and local adjunctive chemotherapy using carbolatin, a second approach was performed using multiple intralesional injections of a 10% formalin solution after an additional surgical debulking. This technique resulted in progressive regression of the mass. No tumour recurrence was observed during a follow up period of 22 months, and only mild local adverse effects were reported. This case suggests that intralesional formalin injection may represent a simple and cost-effective adjunctive treatment option for selected intraoral tumours in horses when conventional approaches are limited.

Keywords

horse, adjuvant therapy, oral tumours, outcome, treatments

Introduction

Oral masses are an uncommon presentation in equine practice, with gingival tumours being particularly rare compared to other species (Bienert- Zeit et al., 2022). Squamous cell carcinoma (SCC) is the most frequently reported primary oral neoplasm in horses and can affect any mucosal surface (Luff et al., 2023). Other reported tumours include mesenchymal tumours such as fibroma, ossifying fibroma, fibrous dysplasia, osteoma, fibrosarcoma, sarcoids, osteosarcoma and myxoma (Bienert- Zeit et al., 2022; Bush et al., 2007; Kodaira et al., 2010; Munday et al., 2024; Nottle et al., 2021). Dental tissue- derived tumours as

peripheral odontogenic fibroma (Hollis, 2021), among others, have also been described (Bienert- Zeit et al., 2022; Morgan et al., 2019). Some non- neoplastic growths such as gingival fibrous hyperplasia (Handy et al., 1993) or developmental disorder of bone as fibrous dysplasia can mimic a neoplastic process.

Clinical signs associated with oral masses vary and may include ptyalism, halitosis, tongue protrusion, quidding, dysphagia, nasal discharge containing food material, anorexia, weight loss, stridor and oral bleeding (Dixon & Gerard, 2019). Radiography remains the first- line imaging modality in the exploration of head disorders owing to its wide availability, ease of use and low cost. Because some tumours infiltrate both bone and soft tissues and because the inherent superimposition associated with radiography limits the accurate assessment of individual structures, cross- sectional imaging such as computed tomography (CT) is often necessary for precise tumour delineation and surgical planning (Manso- Díaz et al., 2015; Stieger- Vanegas & Hanna, 2022). Definitive diagnosis requires histopathological examination.

Treatment options include medical management, such as local and/or systemic chemotherapy and radiation therapy, as well as surgical excision. Complete surgical excision in equids is often challenging because anatomy results in difficult and limited access; combining therapies can improve long- term outcomes (Berryhill et al., 2022).

Gingival fibroma (GF) is a rare, benign and typically solitary tumour characterised by a firm and well- demarcated mass. Histologically, it consists of well- differentiated spindle- shaped cells embedded in a collagenous matrix. The terms fibromatous epulis and peripheral odontogenic fibroma are sometimes used as synonyms (Bienert- Zeit et al., 2022). Gingival fibroma is common in dogs and occasionally reported in cats but is very rare in horses (Hollis, 2021). These lesions are generally non- painful, although they may cause discomfort if the overlying epithelium becomes inflamed or ulcerated, or if the mass is large enough to interfere with mastication. Complete excision is required to reduce the risk of recurrence (Schade et al., 2021).

Formalin has been used in equine medicine for haemorrhage control (Moreno et al., 2021), treatment of progressive ethmoidal haematoma (Marriott et al., 1999), management of epidermal inclusion cysts (Frankeny, 2003), congenital parotid salivary duct atresia (Williams & Nickels, 2020), maxillary bone cysts (Van Delft et al., 2018) and subepiglottic cysts (Dougherty & Palmer, 2008). However, to the best of our knowledge, its use as an adjunctive therapy after tumour debulking has not been previously described.

This case report describes the successful application of formalin following surgical debulking of a large space- occupying GF in a mare.

Case description

History and clinical findings

A 25- year- old, 356 kg saddlebred mare was referred for evaluation of a swelling on the left mandible and multiple intraoral masses. The owner first noted swelling and mild oral bleeding approximately 1 month before presentation at the clinic.

On admission, the mare was alert, with a body condition score of 5/9 (Henneke scale). Vital parameters were within normal limits. Thoracic and abdominal auscultation was unremarkable.

External examination of the head (inspection and palpation) revealed a firm, non- painful deformity of the left mandibular arcade, rostral to the masseter muscle, near levelled to the dental table. The left mandibular lymph nodes were hypertrophic on palpation.

Oral endoscopy performed under standing sedation, using a bolus of detomidine hydrochloride (Domidine® 10 mg/mL) at 0.01 mg/kg bwt, i.v. and butorphanol tartrate (Butomidor® 10 mg/ mL) at 0.01 mg/kg bwt, i.v., revealed a wave mouth more accentuated on the left side, multiple diastemata and peripheral and infundibular caries not associated with clinical signs. A large, pink to reddish, exophytic and multilobulated mass, approximately 5 × 9 cm in size, emerged from the gingiva in the interdental space between the left mandibular molar teeth 310 and 311 (Figure 1). It extended lingually and buccally, deforming the cheek. It also partially obscured teeth 310 and 311, preventing proper evaluation during the initial oral examination. A biopsy of the mesial aspect of the mass was taken with scissors.

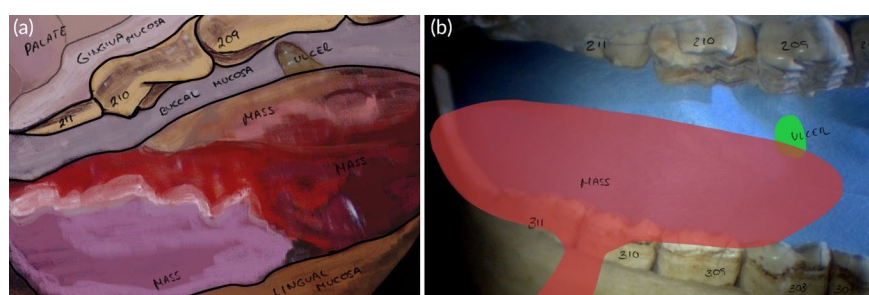


Figure 1 (a) Schematic drawing of an intraoral endoscopic view showing a large, pink to reddish, granulomatous, ulcerated and bleeding mass arising from the gingiva along the left mandibular arcade. (b) Schematic illustration of the mass on a model of the equine head, based on the intraoral endoscopic view, highlighting the extent of the lesion and its association with teeth 310 and 311.

Ancillary examinations

Dorsoventral, latero- lateral and multiple oblique radiographs of the left mandible revealed a lytic well- delineated bone lesion deeply affecting the body of the left mandible, communicating with the oral cavity and extending dorsally as a soft- tissue mass invading the space between teeth 310 and 311 (Figure 2).

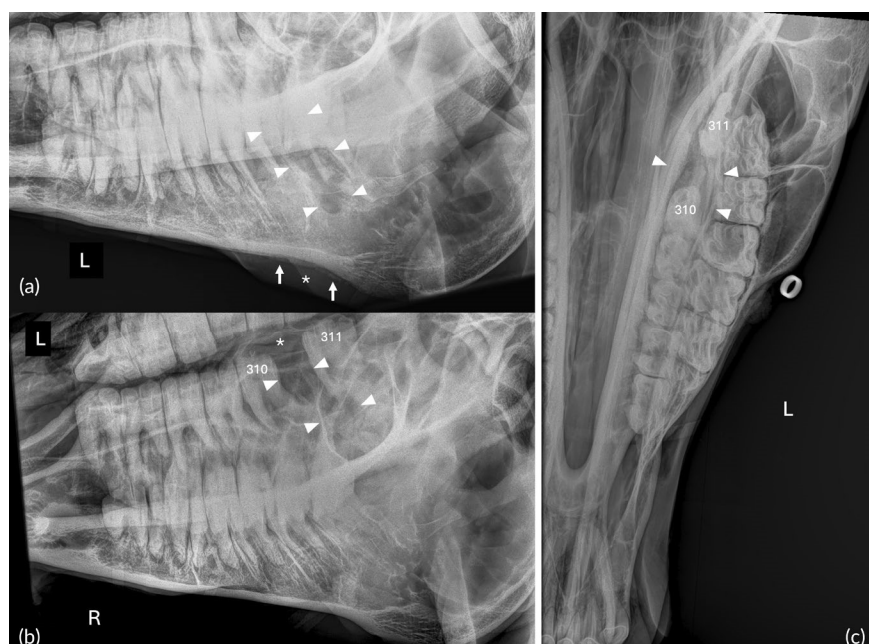


Figure 2 (a) Right ventrolateral left dorsolateral oblique, (b) left ventrolateral right dorsolateral oblique and (c) focused dorsoventral radiographic images of the mandible at the initial examination. Well- delineated pressure lysis affecting the left mandible is visible, separating teeth 310 and 311 and communicating with oral cavity dorsally (a–c, white arrowheads). Note the few radiopaque palisading periosteal bone production at the ventral border of the left mandible (a, arrows) with concurrent subcutaneous soft- tissue swelling (a, asterisk). A soft- tissue mass invading bone is visible protruding at the occlusal surface of the left mandibular dental table (b, asterisk).

Concurrent aggressive periostitis and soft- tissue swelling were visible at the ventral aspect of the mandible. Transbuccal ultrasonography of the left mandibular region identified a large, infiltrative, vascularised, partially mineralised soft tissue mass originating from the oral cavity, causing extensive mandibular bone lysis (Figure 3). Left mandibular and retropharyngeal lymphadenopathies were detected. An expansile soft-tissue tumour invading bone and creating a diastema between the teeth of the left mandible was considered most likely.

Histopathology results were inconclusive. Therefore, additional biopsies were obtained during surgical resection.

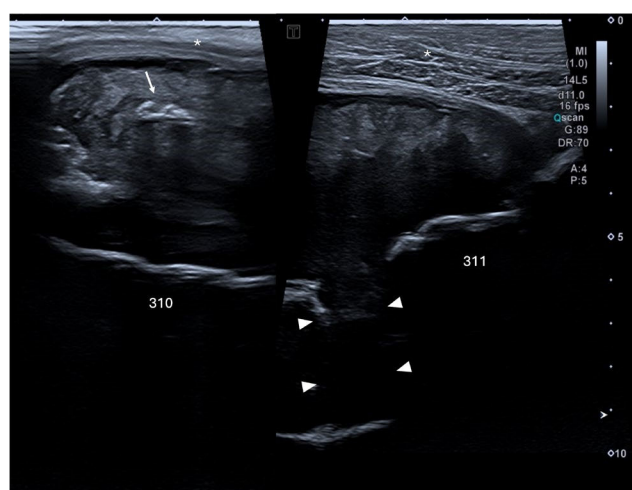


Figure 3 Two adjacent transbuccal ultrasonographic images of the mass involving the left mandibular region with rostro- caudal orientation. A large well- delineated grossly ovoid heterogeneous soft- tissue mass protruding laterally to the mandibular cheek teeth is visible. Note dystrophic mineralisation foci within the mass (arrow). Deep infiltration of the mass between teeth 310 and 311 with lysis of the left mandible and penetration of the echoes is identified (arrowheads). Mass effect characterised by lateral displacement and compression of the superficial buccinator and masseter muscles is observed (asterisk). Rostral is on the left side of the image.

Surgical management

Preoperatively, an intravenous catheter was placed in the left jugular vein, and penicillin (22.000 IU/kg bwt, i.m.; Peni- kel® 300.000 I.U./ mL) and phenylbutazone (2.2 mg/kg bwt, i.v.; Fenylbutazone® 20%) were administered. The mare was premedicated with acepromazine maleate (0.05 mg/kg bwt, i.m.; Tranquinervin® 10 mg/mL) and xylazine (0.6 mg/kg bwt, i.v.; Nerfasin® Vet 100 mg/mL).

The mare was induced with ketamine (2.2 mg/kg bwt, i.v.; Ketexx® Vet 100 mg/mL) and midazolam (0.06 mg/kg bwt, i.v.; Dormazolam® 5 mg/mL), and the trachea was intubated via the nasotracheal route. At the beginning of anaesthesia, a bolus of triple drip (ketamine, guaifenesin and xylazine) was administered to achieve an adequate depth of anaesthesia. The mare was then maintained with sevoflurane (Sevotek® 1000 mg/g) vaporised in an air/oxygen mixture. The mare was positioned in sternal recumbency using an Anderson's sling. Lactated Ringer's solution was administered as a continuous intravenous infusion at

5 mL/kg/h. Invasive arterial blood pressure was monitored via catheterisation of the auricular artery, allowing continuous monitoring of arterial pressure and oxygenation through arterial blood gas analysis.

A left mandibular nerve block was performed using a mixture of 10 mL of mepivacaine hydrochloride (Mepidor® 20 mg/mL) and 10 mL of lidocaine hydrochloride (Laocaine® 20 mg/mL). The size (approximately 5 × 9 cm), depth, location and configuration of the mass, together with oral anatomy, made surgical access very challenging. The mass was surgically debulked using a combination of long- handled heavy mayo scissors and a homemade thread saw consisting of a No. 2 polyglactin 910 suture (coated Vicryl® 2 V- 40 JV1937) mounted through an aluminium tube. The teeth 310 and 311 were extracted due to severe instability that was noticed intraoperatively. The root of the mass was found deeply infiltrated into the interdental space and was debrided as much as possible using a long- handled scalpel and a tenotome because its large, fixed blade reduced the risk of breakage. At the end of the surgery, the bed of the mass and the remaining tissues were infiltrated as deeply as possible with an emulsion of carboplatin (carboplatin Fresenius kabi® 10 mg/mL) and medical sesame oil (Thermo scientific sesame oil® 250 mL), until tissue saturation was achieved, to maximise the local chemotherapeutic effect.

Anaesthesia proceeded uneventfully, and recovery was performed using a rope- assisted technique. Transient ataxia was observed post- operatively, most likely associated with intraoperative positioning and head hyperextension. Clinical signs resolved within 48 h following short- term corticosteroid therapy with dexamethasone (0.05 mg/kg bwt, i.m., q/24 h; Dexashot® 2 mg/mL) for 2 days.

Postoperatively, penicillin procaine (22.000 IU/kg bwt, i.m. q/12 h; Peni-kel® 300.000 IU/mL) and phenylbutazone (2.2 mg/kg bwt, p.o., q 12 h; Chanazone® 1 g) were continued for 4 days. The mare was fed a high- quality forage mix (Hartog Senior®) during hospitalisation and remained comfortable after surgery. The mare was discharged from the clinic 4 days after surgery with instructions to monitor for swelling, ptyalism, appetite, halitosis or abnormal discharge.

Histopathology and final diagnosis

Histopathological analysis of six tissue fragments (3–7 cm) collected during the surgery revealed an ulcerated mesenchymal proliferation consistent with a gingival fibroma. The lesion was extensively ulcerated and covered with thick necrotic cellular material. Short segments with hyperplastic and irregular epithelium were present. The mass consisted of a proliferation of small, fusiform mesenchymal cells arranged in relatively straight, intersecting bundles with a collagenous stroma, extending through the full thickness of the lesion. The nuclei were small, ovoid to spindle shaped, and mitosis figures were absent (Figure 4a). Areas with isolated bone deposits were also present in one fragment, separated by connective tissue with few cells (Figure 4b).

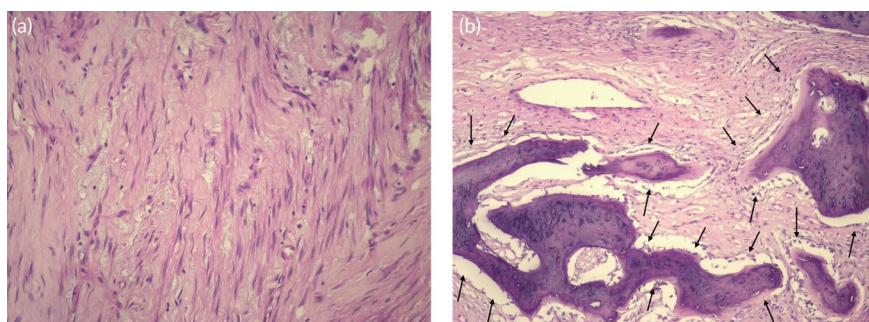


Figure 4 Two histopathological images of the mass using the haematoxylin and eosin staining technique (20×). (a) Proliferation of small spindle cells without atypia, arranged in bundles within a collagen matrix. (b) Focal presence of few mature, isolated, calcified bone deposits (black arrow), separated by sparsely cellular connective tissue.

Postoperative evolution—treatment with formalin and outcome

At the recheck 3 weeks later, proliferative exophytic tissue was filling the alveoli of teeth 310 and 311 (Figure 5a). Its surface appeared irregular, with tissue proliferation along the gingival margin, raising the suspicion of recurrence. A second application under standing sedation of carboplatin in sesame oil was then performed until tissue saturation was achieved.

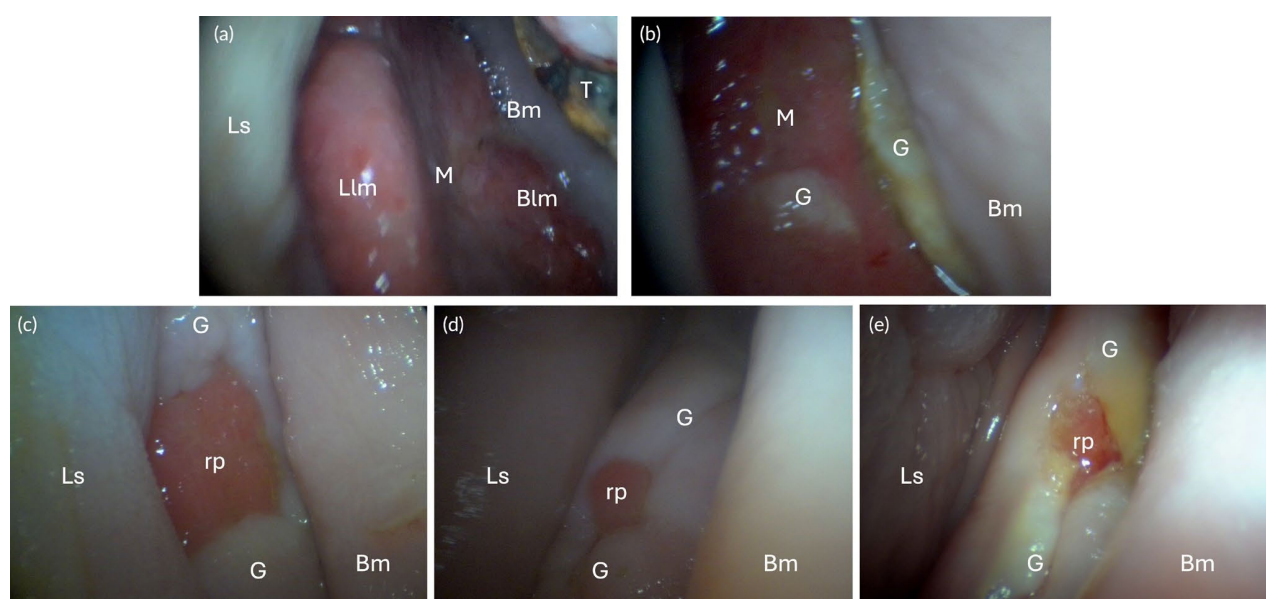


Figure 5 Intraoral endoscopic monitoring during follow- up. (a) Surgical site after mass resection and intralesional cisplatin injection. (b) Marked regression of the lesion following intralesional formalin injection. (c) Further regression of the mass 2 months after formalin re- injection. (d) Normal- appearing gingiva with mild residual reddish discoloration 11 months after the first formalin injection. (e) No changes observed with the mild reddish discoloration 11 months after the last follow- up. Blm, buccal lobe of the mass; Bm, buccal mucosa; G, gingiva; Llm, lingual lobe of the mass; Ls, lingual surface; M, mass; rp, residual pink discoloration; T, teeth.

One month later, despite local chemotherapy, the mass continued to increase in size and extend from lingual to buccal aspects of the gingival margin. Consequently, a new debulking of the mass was performed on both the lingual and buccal aspects under standing sedation. Additionally, 60 mL of 10% neutral buffered formalin (4% formaldehyde) was injected using a 19G butterfly catheter under endoscopic buccal guidance into multiple sites at the base of the mass to induce necrosis of tissue that was not surgically accessible. The mare was discharged on the same day as the surgery.

One month after last surgical treatment, the mare maintained a normal appetite, with no reported oral bleeding or difficult eating. Oral clinical examination revealed a decreased size of the exuberant tissue. Three- month follow- up radiographic examination showed no progression of compressive bone lysis within the body of the left mandible. Control ultrasonographic examination revealed a significant reduction in the size of the mass (2 × 3 cm) compared with the initial examination (9 × 5 cm).

Three months after the previous follow- up examination, the mare presented with halitosis. Oral examination identified again an exuberant tissue in the region of the alveolar space of tooth 310, although

the mass appeared smaller and less proliferative than on the previous consultations (Figure 5b). A new local injection of 20 mL of formalin was performed under standing sedation.

One month later, oral examination showed a marked reduction in the size of the mass (Figure 5c). However, a mandibular abscess was identified on the left cheek, likely related to the previous formalin injection. The abscess was drained using a No. 11 scalpel blade and debrided with a curette, and systemic treatment with oral phenylbutazone and doxycycline was initiated, in combination with local wound care consisting of flushing and removal of discharge.

Following complete resolution of the abscess, a follow-up examination 3 months later confirmed favourable clinical progression. The gingiva was firm and fully covering the alveoli with a smooth, regular, non-exuberant tissue (Figure 5d). The affected area could only be distinguished from the normal gingiva by its slightly reddish colour. Follow-up radiographic examination of the left mandible revealed no evidence of disease progression in comparison with the last radiographs performed 10 months earlier.

The last clinical assessment was conducted 22 months after the last formalin treatment. The mare continued to eat normally and had gained 60 kg of weight. At oral examination, no evidence of recurrence was observed. The gingiva appeared normal, except for a small area of approximately 0.5 cm in diameter that remained slightly more reddish compared to the surrounding normal gingiva (Figure 5e).

Discussion

This case describes an unusual low-grade aggressive expansile mesenchymal proliferative mass invading bone with focalised mature bone deposits, localised in the caudal aspect of the horizontal branch of the mandible, consistent with a fibroma, in an aged mare, treated by surgical debulking and adjuvant therapy. Differential diagnosis in horses includes low-grade fibrosarcoma (Bass et al., 2017; Horbal & Dixon, 2016), fibromatous epulis (Hollis, 2021), fibrous dysplasia (Knottenbelt et al., 2015; Nottle et al., 2021), ossifying fibroma (Kodaira et al., 2010) and focal fibrous hyperplasia (Handy et al., 1993). Equine odontogenic tumour was considered less likely. Three cases of GF have been described in horses (Hablolvarid et al., 2012; Leal et al., 2014; Schade et al., 2021). The clinical signs observed in this case, such as oral bleeding and facial asymmetry, are consistent with those typically associated with oral tumours in horses (Knottenbelt & Kelly, 2011).

The macroscopic characteristics of the mass were comparable to those reported by Hablolvarid et al. (2012) and Schade et al. (2021), being pink, firm and smooth in appearance. In these reports, the tumours were located near the first premolar or in the rostral mandible. Similarly, in dogs, GF are most commonly located in the rostral aspect of the maxilla, followed by the body of the mandible (Fiani et al., 2011). Surgical excision in these regions is generally easier to perform due to the rostral location and, in dogs, the greater oral accessibility. In the present case, however, the lesion was located more caudally, between teeth 310 and 311, within the typical tubular-shaped equine oral cavity. This represents a less common location for such tumours and significantly limits surgical access.

Computed tomography examination is useful for extension work-up and/or treatment planning when surgical excision is indicated, as it allows detailed assessment of the underlying bone (Hackett & Baxter, 2008; Manso-Díaz et al., 2015). In the present case, CT examination was not performed due to financial constraints, and the diagnosis was established based on radiographic, ultrasonographic and

histopathological findings. The absence of a CT examination was considered of limited impact, as mandibulectomy was not an option for the owners.

Ideally, treatment of GF requires complete surgical excision. Broad-based or ossified lesions may require more aggressive surgery, including bone contouring at the excision site. Partial mandibulectomy, either rostral or distal, has been described for the management of oral tumours (Carmalt & Linn, 2013; Cousty & Tricaud, 2014; Mendez-Angulo et al., 2014). However, in this case, the owner declined this more invasive and technically demanding procedure.

Intraoral resection and chemotherapy of the mass was then performed in this case. As previously described for the removal of intraoral masses (Bienert-Zeit et al., 2022), complete excision can be challenging at this anatomical location, thereby increasing the risk of recurrence. Due to the lack of response to carboplatin and the persistence of the mass, administration of formalin was performed in an attempt to promote regression of the lesion and facilitate healing.

The mechanism of action of formalin, an aqueous solution of formaldehyde, has been described in both human and veterinary literature. In equine medicine, formalin has been shown to cause tissue dissection and coagulation through protein denaturation (Schumacher et al., 1998). These effects are primarily related to its cytotoxic action on endothelial and stromal cells, leading to local tissue necrosis and reduced vascular supply.

These properties may explain its efficacy in conditions such as progressive ethmoidal haematoma (Marriott et al., 1999) and may account for the beneficial effect observed in the present case, particularly in lesions that cannot be completely excised. However, formaldehyde is a known carcinogenic compound in humans (Protano et al., 2021), and its use should therefore be carefully considered. Although no direct studies exist linking it specifically to cancer in horses, it should still be used with caution regarding dose, frequency and local tissue exposure.

Additionally, several complications have been reported following intralesional formalin injection, depending on the site of administration and proximity to surrounding structures. Reported adverse effects include local healthy tissue necrosis, inflammation, neurological signs and abscess formation (Frees et al., 2001; Williams & Nickels, 2020). However, mortality potentially associated with formalin administration has been reported in at least one horse, although a direct causal relationship could not be definitively established (Moreno et al., 2021).

In the present case, the only complication observed was the development of a cheek abscess, which was successfully managed by drainage and debridement without further sequelae. This suggests that, when used judiciously and in anatomically less critical regions such as the mandible, intralesional formalin administration may represent a relatively safe adjunctive treatment.

In conclusion, in cases where GF are difficult to access for complete excision, formalin injection may serve as a useful adjuvant therapy to surgical debulking. Furthermore, this minimally invasive approach is economically advantageous compared to more invasive procedures such as mandibulectomy, potentially reducing treatment costs and postoperative morbidity. No major complications were observed in this case. However, further studies, ideally with a larger sample size, are warranted to confirm the safety and efficacy of this approach.

Author contributions

S. Jolly: Writing – review and editing; visualization; validation; investigation. **G. de la Rebière de Pouyade:** Methodology; visualization; writing – review and editing; project administration; validation; investigation; supervision; conceptualization. **G. Caballero Delgado:** Writing – original draft; writing – review and editing; visualization; methodology; conceptualization; validation; investigation. **B. Román Durá:** Validation; visualization; writing – review and editing; investigation. **A. Salciccia:** Visualization; validation; writing – review and editing; investigation. **A. Charles:** Visualization; writing – review and editing; validation; investigation. **S. Grulke:** Conceptualization; visualization; writing – review and editing; investigation; validation.

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Conflict of interest statement

The authors declare that they have no competing interests.

Data availability statement

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Ethics statement

The report is based on a clinical case presented to our hospital and was not subject to ethical approval. The owner gave full consent for publication.

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