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Hemimandibulectomy for treatment of an ameloblastoma in a 13-year-old Holsteiner gelding

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Summary: This case report describes the treatment and outcome of a 13-year-old Holsteiner gelding presented to the Equine Hospital, University of Zurich, because of a rapidly growing ameloblastoma located in the rostral aspect of the left mandible. Radiography and computed tomography were used to localise the tumour and plan the surgery. The tumour was removed via hemimandibulectomy, and at the six-month follow-up, signs of recurrence were not evident. However, mild tongue protrusion was observed as a side effect of incisor removal. Histological evaluation of the tumour confirmed ameloblastoma in agreement with the initial biopsy diagnosis. Ameloblastoma is rare in horses and the prognosis is good, provided that complete surgical resection can be achieved.

Keywords: horse, ameloblastoma, hemimandibulectomy

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Introduction

Odontogenic tumours are rare in domestic animals and descriptions are limited to three older reports (*Mensa* 1938, *Gorlin* et al. 1963, *Cotchin* 1977) and two more recent textbook entries (*Knottenbelt* and *Kelly* 2010, *Munday* et al. 2016). In a review of 1,230 oral tumours in domestic animals, *Gorlin* et al. (1963) reported that 267 appeared to be of dental origin. The majority (253) were classified as fibromatous epulis of periodontal origin, now called odontogenic fibroma, which is the most common oral tumour in dogs. Other studies found that odontogenic tumours occur mainly in dogs and cats and are rare in other species (*Munday* et al. 2016).

Fig. 1 The appearance of the ameloblastoma when it was first noticed. | *Das Ameloblastoma als es das erste Mal bemerkt wurde.*

The classification of odontogenic tumours in veterinary medicine is based on the system used in human medicine, which has changed over the years. The 2005 classification system was complex and therefore simplified in 2017. Since then, odontogenic tumours are classified into malignant and benign tumours. The benign tumours get further classified according to their histological character into epithelial, mesenchymal (ectomesenchymal), and mixed odontogenic tumours (*Wright* and *Vered* 2017). Table 1 provides an overview of the most important odontogenic tumours in horses based on the current WHO classification.

The number of odontogenic tumours reported in horses is too low to determine the single most common type (*Morgan* et al. 2019), but several case reports provided an overview of the most common types (*Kutzler* et al. 2007, *Koch* et al. 2014, *Mendez-Angulo* et al. 2014, *Smith* et al. 2017, *Morgan* et al. 2019). A thorough clinical examination and diagnostic imaging are of paramount importance for the early detection of odontogenic tumours; however, histological examination is usually needed for tissue characterisation of the neoplasm (*Morgan* et al. 2019).

The following case report describes the diagnosis, treatment and histological characterisation of an ameloblastoma located in the rostral aspect of the mandible in a horse.

Case history

A 13-year-old Holsteiner gelding was referred to the Equine Hospital of the University of Zurich because of a mass located between the incisors and canine tooth of the left mandible. According to the owner, the mass had grown to a diameter of approximately 2 cm in about two weeks. The primary care veterinarian had taken radiographs, extracted the incisor 303 and obtained a biopsy sample of the mass for histological evaluation, which revealed an ameloblastoma.

Clinical findings

At the time of admission, the gelding was in good general health. Physical examination revealed a round mass, where incisor 303 had been extracted, and a buccal bulge in the area of the canine root (304) (Figure 1). Palpation of the gingiva around the mass did not elicit pain.

Diagnostic imaging

Radiography

The gelding was sedated with detomidine (0.015 mg/kg bwt i.v.)[1] and butorphanol (0.02 mg/kg bwt i.v.)[3] to obtain intraoral (ventrodorsal oblique 0°/-60° view) and lateral (90°/0° view) radiographs of the head. The radiographs showed a round structure with soft-tissue density and a diameter of 3.8 cm and several areas of slightly increased mineralisation in the incisive bone (Figure 2). Widening of the alveoli of incisors 302 and 304 and a prominent smooth periosteal reaction on the buccal side of the alveolar bone of the canine tooth were seen.

Fig. 2 Intraoral radiograph (ventrodorsal oblique 0°/-60° view) of the incisive bone: The lower corner incisor (303) is missing. The white arrows point to a round structure with soft-tissue density. Distinct expansion of the alveoli of teeth 302 and 304 (*) is evident. A prominent smooth periosteal reaction is seen on the buccal side of the alveolar bone of the canine tooth (black arrows). | *Intraorales Röntgenbild (ventrodorsal schräg 0°/-60°) des Os Incisivum: An der Stelle des schon entfernten 303 ist eine rundliche, weichteildichte Struktur sichtbar (weisse Pfeile). Zudem ist die Erweiterung der Zahnalveolen des 302 und 304 auffällig (*). Die Zahnalveole des Caninus zeigt bukkal periostale Reaktionen (schwarze Pfeile).*

Computed tomography

Computed tomography (CT) of the affected area was undertaken with the horse standing to obtain more detailed information about the tumour and to plan for possible surgical removal. The gelding was sedated with detomidine (0.02 mg/kg bwt i.v.)[1], butorphanol (0.02/kg bwt i.v.)[3] and, because the sedation was not deep enough, xylazine (0.5 mg/kg bwt i.v.)[3]. The CT images showed a large mass, approximately 4 cm in

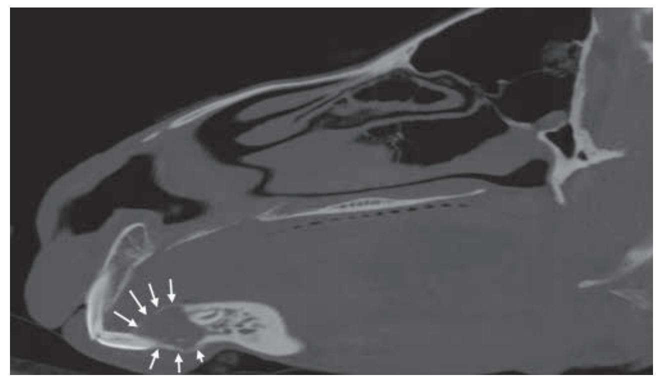

Fig. 3 Computed tomographic image of the mandible in the sagittal plane in the gelding with ameloblastoma. Focal lysis and swelling between the incisive teeth and the canine tooth (304) (white arrows) are evident. | *Fokale Lyse und Schwellung zwischen des Incisivum und des Caninus (weiße Pfeile) sind sichtbar.*

Table 1 Overview of the most important odontogenic tumours in horses. | *Übersicht über die wichtigste odontogene Tumoren bei Pferden.*

Odontogenic tumors of the horse	Other used terms
Epithelial odontogenic tumors	
Ameloblastom	Adamantinoma
	Adenocatoid ameloblastoma
Ameloblastic carcinoma*	Basal cell carcinoma
Mixed odontogenic tumors	
Ameloblastic fibroma	Fibroameloblastoma
Complex odontoma	
Compound odontoma	
Mesenchymal odontogenic tumors	
Cementoma, cementoblastoma	Periapical cemental dysplasia
	Gigantiform cementoblastoma
	Benign cementoblastoma
	Cementifiying fibroma
Odontogenic myxoma	
Odontogenic myxosarcoma*	

*malignant

diameter, that extended from the root of 301 to the affected root of the canine tooth (Figure 3). Focal lysis with swelling and destruction of cortical and spongious bone was seen. The buccal aspect of the canine tooth had a wide smooth periosteal reaction but caudally, the cortical bone over of the root tip was intact. No other abnormalities were seen. A 3D reconstruction of the CT images was carried out to better determine whether the tumour could be removed surgically (Figure 4). The distance between the symphysis and the tumour was large enough to justify tumour removal without additional stabilisation of the symphysis. A hemimandibulectomy of the left mandible was therefore recommended to the owner.

Surgical technique

The horse underwent surgery the day after admission to our clinic. Penicillin (30,000 IU/kg bwt i.v.)[3], gentamicin (10 mg/kg bwt i.v. q. 24 h)[4] and phenylbutazone (4 mg/kg bwt i.v. q. 12 h)[3] were administered 30 min before surgery. The horse was sedated with acepromazine (0.03 mg/kg bwt i.m.)[5] followed by medetomidine (0.07 mg/kg bwt i.v.)[4] 20 min later. General anaesthesia was induced with ketamine (2.2 mg/kg bwt i.v.)[6] and diazepam (0.02 mg/kg bwt i.v.)[7] and maintained using isoflurane[7] (Isofluran Baxter®)[8] in oxygen and air and a constant rate infusion (CRI) of medetomidine (0.035 mg/kg/h)[4]. The horse was placed in dorsal recumbency and nasotracheal intubation (Ø 11 mm) was done because of the location of the surgery. A CRI of dobutamine (0.074 mg/kg/h i.v.)[9] and lactated Ringer's solution was administered because the horse had a type II atrioventricular block and hypotension (MAP < 70 mmHG). Ten ml mepivacaine (0.4 mg/kg bwt)[10] was used for mandibular block anaesthesia. The rostral part of the mandible was prepared for aseptic surgery. The lower lip was folded caudally and fixed with stay sutures to better visualise the surgical field. An incision was made in the oral mucosa and subcutaneous tissues sagittally between incisors 301 and 401 and extended over the ventral and dorsal aspect of the mandible and distally around the canine tooth (304). The gingiva was separated and retracted using wound retractors. Sagittal and laterolateral cuts were made through the bone with an oscillating saw. The rostral part of the left mandible, including the teeth 301 and 302, the alveolar bone of the previously extracted 303 and parts of the alveolar bone of the affected canine tooth were removed. A Bein elevator and a gouge were used to remove the remaining canine tooth. The alveolar socket of 304 was curetted and the medullary cavity extended to ensure removal of all abnormal tissue (Figure 5). The large cavity that extended to the mandibular canal was then closed by apposition of the lingual and labial mucosa, beginning caudally and moving rostrally, using 2–0 monofilament absorbable glycomer suture material (Biosyn) in a continuous suture pattern. An area of mucosa was left open rostrally to allow insertion of a swab that had been soaked in an antiseptic solution (Octenisept) into the cavity. The swab was secured to the mucosa using 0 pseudomonofilament polyamide suture material (Supramid) in a cruciate suture pattern. Intra-oral radiographs were obtained immediately after surgery to determine whether the tumour had been completely removed (Figure 6). Recovery from anaesthesia was uneventful. The resected part of the mandible and canine tooth were evaluated histologically to classify the mass and determine whether the surgical margins were tumour-free.

Postsurgical management

Flunixin meglumine (1.1 mg/kg bwt i.v. q. 24 h)[2] was administered postoperatively for two days. Penicillin (30,000 IU/kg bwt i.v. q.6 h)[3] and gentamicin (10 mg/kg bwt i.v. q.24 h)[4] were administered for two days. The day after the surgery, the gelding had a good appetite and was fed soaked grass hay and mash. Radiographs taken 2 days postoperatively showed no visible remnants of the extracted tooth root. The mandib-

Fig. 4 3D reconstructed computed tomographic scan of the head showing the location and size of the ameloblastoma (white arrows). | *Die 3D Rekonstruktion der Computertomographie des Kopfes zeigt das Ausmaß des Ameloblastoms (weiße Pfeile).*

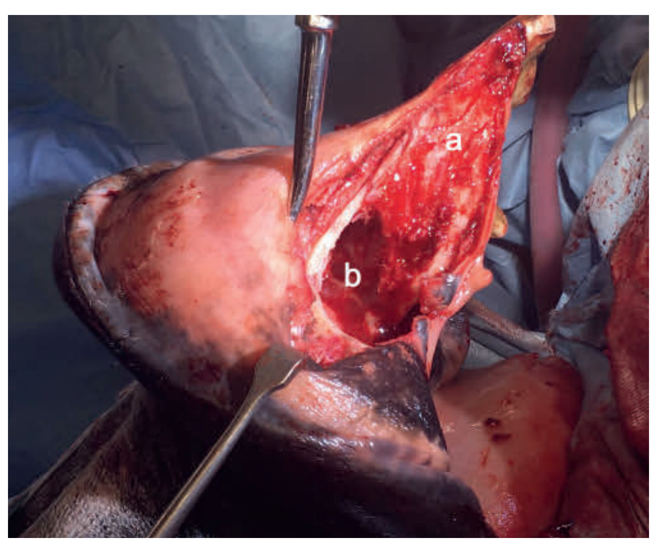

Fig. 5 The appearance of the wound after complete removal of the ameloblastoma. The incisive teeth on the right side of the mandible (a) and the cavity remaining after tissue removal (b) are evident. *Die Wunde nach Entfernung des Ameloblastoms. Die verbliebenen Incisivi auf der rechten Seite der Mandibel (a) und die Wundhöhle (b) sind sichtbar.*

ular symphysis appeared stable. The original swab was exchanged, the suture line was intact and the gelding was discharged in good general condition.

Aftercare instructions included continued analgesia with flunixin meglumine (1.1 mg/kg bwt sid p.o.)[9] for the next 5 days. In addition, the horse was fed a diet of soaked pellets (mash)

Fig. 6 Postsurgical intraoral radiograph of the remaining incisive bone showing the complete removal of the tumour and the intact mandibular symphysis. | *Postoperatives intraorales Röntgenbild des Os Incisivum zeigt die komplette Entfernung des Tumors und die intakte Mandibularsymphyse.*

Fig. 7 Photograph showing the healed wound and remaining incisive teeth (a) 6 months after hemimandibulectomy. | *Verheilte Wunde entlang der verbliebenen Schneidezähnen (a) 6 Monate nach der Hemimandibulektomie.*

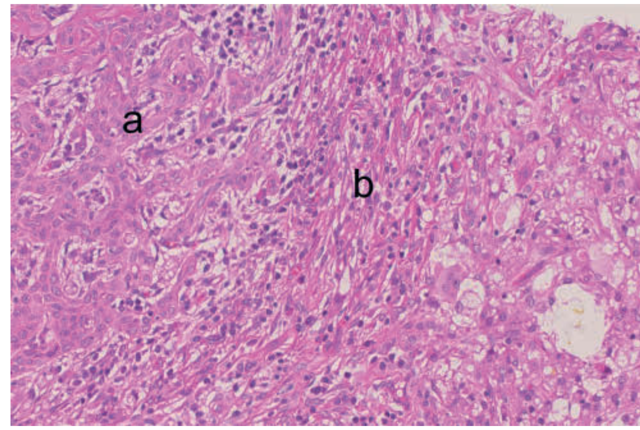

Fig. 8 Histological section of the ameloblastoma showing cords of epithelial cells (a) and heterogeneous tissue with epithelial cells and cells that resemble the stellate reticulum (b). (Haematoxylin and eosin stain; 40 × magnification). | *Histologischer Schnitt durch das Ameloblastom zeigt Stränge von infiltrierenden Epithelzellen (a) und chaotisches/heterogenes Gewebe mit Epithelzellen und Zellen, die dem Stellate reticulum ähneln (b). (H&E, 40-fache Vergrößerung).*

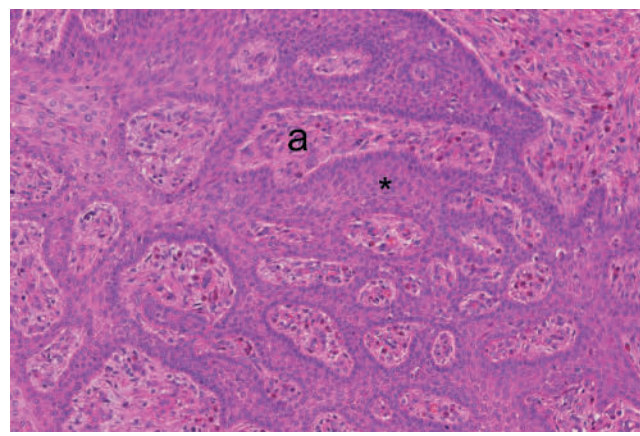

Fig. 9 Histological section of the ameloblastoma showing hyperplasic epithelial cells (*) surrounding the stellate reticulum (a). (Haematoxylin and eosin stain; 20 × magnification). | *Histologischer Schnitt durch das Ameloblastom mit hyperplastische Epithelzellen (*) umgeben von Stellate reticulum (a). (H&E, 20-fache Vergrößerung).*

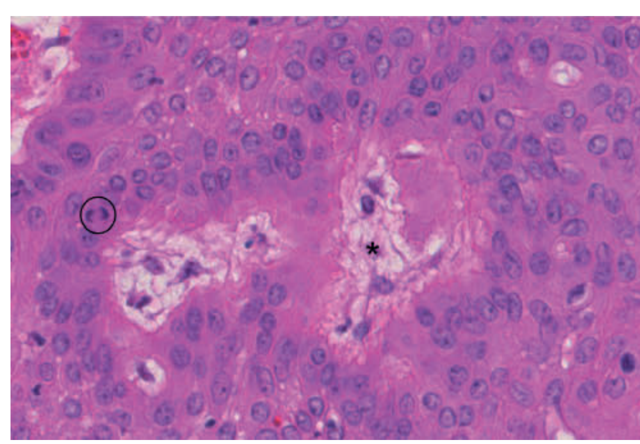

Fig. 10 Histological section of the ameloblastoma showing the basal epithelium with a mitotic figure (circle) and the stellate reticulum (*). (Haematoxylin and eosin stain; 80 × magnification). | *Histologischer Schnitt durch das Ameloblastom zeigt basales Epithel mit Mitosefiguren (Kreis) und Stellate reticulum (*). (H&E, 80-fache Vergrößerung).*

and soaked grass hay with exclusion of treats, such as carrots and dry bread, for 1 week. The primary care veterinarian carried out follow-up examinations every 4–5 days to change the swabs and monitor the suture line. No complications were reported.

Six-month follow-up

Six months after surgery, the owner reported that the wound had healed successfully (Figure 7) and the gelding was in good general health and had returned to its previous level of activity as a pleasure riding horse. Oral function was normal despite hemimandibulectomy and only mild protrusion of the tongue was observed.

Histological analysis

Histological evaluation of the mass removed at surgery revealed a zone of neoplastic cells and fibrous tissue surrounded by alveolar bone. The neoplastic zone contained cords of epithelial cells and heterogeneous tissue composed of epithelial cells and cells simulating the stellate reticulum (Figure 8). Mild diffuse infiltration of eosinophils in the subepithelial layer of the stellate reticulum was seen. This was surrounded by palisading basal cells, which is typical of ameloblastoma (*Munday* et al. 2017) (Figure 9). The epithelial cells appeared hyperplastic, and mitotic figures were seen (Figure 10). The surgical margins were analysed to be tumour-free.

Discussion

Ameloblastomas originate from odontogenic ectoderm, which develops into the enamel organ. They usually involve the mandible but have been described in the maxilla of old horses (*Knottenbelt* and *Kelly* 2010) and a foal (*Smith* et al. 2017). Ameloblastomas are benign tumours that are locally invasive, rarely metastatic (*Rosol* et al. 1994, *Crabill and Schumacher* 1998) and display rapid or slow growth (*Rosol* et al. 1994, *Morgan* et al. 2019). Clinically, ameloblastomas often appear as firm swellings that lead to malformation of the affected dental arcade (*Knottenbelt* and *Kelly* 2010). Ameloblastomas located in the maxilla may expand into surrounding structures such as the maxillary sinus (*Munday* et al. 2017).

The WHO (*Wright* and *Soluk-Tekkeşin* 2017) has classified ameloblastomas into four main categories in humans: conventional ameloblastoma, unicystic ameloblastoma, extraosseous/peripheral type and metastasizing ameloblastoma. Each type can be further differentiated into histopathological subtypes.

However, detailed differentiation has not been used regularly, particularly in veterinary medicine. The use of tumour markers can aid in diagnosis when tissue samples are of poor quality, and immunohistochemical evaluation has been used in human medicine. The expression of CK 5 and CK 14, which are markers of ameloblastoma in human medicine (*Vigneswaran* et al. 1993), has been used to identify this tumour in horses (*De Cock* et al. 2003).

Other types of odontogenic tumours may also occur in horses. Although rare, ameloblastic carcinoma is an aggressive and destructive malignant odontogenic tumour. Histologically, it is characterised by highly invasive growth and cells with a high nucleus-to-cytoplasm ratio and high mitotic index along with the histological features of conventional ameloblastoma (*De Cock* et al. 2003). Ameloblastic fibroma and complex and compound odontoma are neoplasms with epithelial and ectomesenchymal (odontoblasts, cementoblasts, osteoblasts, fibroblasts) components. Ameloblastic fibroma is the least differentiated tumour, and compound odontoma has the most complete odontogenic maturation (*Knowles* et al. 2010). The best known mesenchymal odontogenic tumour is the cementoma. However, it is important to note that cementoma is used for any one of the following three lesions in veterinary medicine: the true neoplasm (cementoblastoma), a dysplastic lesion (periapical cemento-osseous dysplasia) and a hyperplastic lesion (hypercementosis) (*Bell* and *Soukup* 2014). The true neoplasm is characterised by proliferation of mesenchymal cells with no or very scarce odontogenic epithelium (*Munday* et al. 2017). Odontogenic myxoma and odontogenic myxosarcoma are extremely rare in horses and therefore differentiation has not been done (*Munday* et al. 2017).

Radiography is the standard imaging technique used for suspected neoplastic diseases of the head in horses. Radiographs help to rule out abscessation of the tooth root and fractures and support the differentiation of odontogenic tumours from oral neoplasms of non-dental origin. Ameloblastomas appear radiographically as cystic or multi-cavitary structures (*Knottenbelt* and *Kelly* 2010), which are usually not associated with lysis of the affected tooth root (*Koch* et al. 2014). Interpretation of radiographs of the head can be challenging. Computed tomography is a valuable imaging technique when the location of the mass is difficult to determine using conventional radiography or surgical removal is desired. It allows reliable assessment of the extent of the lesion and provides information about the invasiveness of the tumour. However, except the complex odontomas which contains enamel, the appearance of odontogenic tumours on CT images is not pathognomonic (*Morgan* et al. 2019).

Ultrasonography, magnetic resonance imaging (MRI), gamma scintigraphy, endoscopy and haematological and biochemical analyses are other tools that have been used for diagnosis of neoplastic diseases (*Knottenbelt* and *Kelly* 2010). However, only MRI has been shown to aid in the diagnosis and differentiation of odontogenic tumours (*Koch* et al. 2014). Magnetic resonance imaging was also better than CT for determining the extent of tumour-related destruction and the degree of invasiveness (*Koch* et al. 2014). Despite these advantages, MRI is more time-consuming to do and most horses require general anaesthesia, whereas CT can be carried out relatively quickly with the horse sedated and standing.

A definitive diagnosis of ameloblastoma requires histological evaluation. Two main histological characteristics are seen in ameloblastomas: islands of epithelium with basal cell characteristics and cells that represent the stellate reticulum. The central cells (stellate reticulum) are spindle-shaped and appear in dense nests (*Gardner* 1994). However, because odontogenic tumours are rare, pathologists may not have the expertise required for their diagnosis. It is therefore important to ensure good collaboration between the clinician, radiologist and pathologist for a definitive diagnosis. It is also important to note that histological evaluation of tooth structures cannot be done until the specimen has been decalcified, which takes time. Therefore, in some cases, the surgery must be performed to prevent further growth of the tumour before the results of the histological evaluation are available.

The treatment of ameloblastoma is usually surgical removal, depending on tumour location. Surgical removal combined with cryotherapy has been described, especially when clean margins are difficult to obtain (*French* et al. 1974). The prognosis of this tumour depends on whether surgical removal is an option. Conservative treatment can be instituted when surgical removal is not possible. However, expansion of the tumour will eventually interfere with quality of life and euthanasia is then elected (*Knottenbelt* and *Kelly* 2010). This also applies to other odontogenic tumours.

A major limitation of the presented case is that, being a single case, it is not possible to generalise; however, this case suggests that the location, early diagnosis and surgical removal of ameloblastoma play a more important role in the prognosis than tumour classification. This is supported by other case reports, which show that the prognosis is good, provided surgical removal is complete, even in cases with more invasive malignant tumours such as ameloblastic carcinoma (*Reardon* et al. 2017). When complete surgical removal is not possible because of the location or size of the tumour, euthanasia is often required even with benign tumours such as ameloblastoma (*Kutzler* et al. 2007, *Smith* et al. 2017).

Besides general complications that may occur during a surgery, a fracture of the mandibular symphysis is possible after hemimandibulectomy. The more bone from the incisive part is resected, the weaker the mandibular symphysis becomes, increasing the chances of fracture after surgery. However, also a fractured symphysis can have a good outcome (*Mendez-Angulo* et al. 2014). Hemimandibulectomy resulted in successful treatment including retention of normal oral function in the present case.

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Manufacturers' addresses

1 Virbac AG, Opfikon, Switzerland
2 Biokema SA, Crissier, Switzerland
3 Streuli Pharma AG, Uznach, Switzerland
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5 Arovet AG, Dietikon, Switzerland
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10 Sintetica SA, Mendrisio, Switzerland

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