Campylorrhinus lateralis, bilateral **microphthalmia** and **odontoma temporalis** in an Oldenburg foal

Case Report

Campylorrhinus lateralis, bilateral *microphthalmia* and *odontoma temporalis* in an Oldenburg foal

Running head: Congenital cranial anomalies in a foal

C Casteleyn[1], P Cornillie[2], V Tüllmann[2], S Van Cruchten[1] and C Van Ginneken[1]

[1]*Laboratory of Applied Veterinary Morphology, Department of Veterinary Sciences, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp, Wilrijk, Belgium;* [2]*Department of Morphology, Faculty of Veterinary Medicine, Ghent University, Merelbeke, Belgium*

Author's address (for correspondence):

C Casteleyn, Laboratory of Applied Veterinary Morphology, Department of Veterinary Sciences, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp, Wilrijk, Belgium. E-mail: christophe.casteleyn@uantwerpen.be

Highlights:

- We describe a unique case of wry nose, microphthalmia and odontoma in a foal
- The etiology of the wry nose and microphthalmia might be lack of intrauterine space
- The etiology of the odontoma that was located on the temporal crest is less obvious
- The newborn foal probably died by suffocation induced by the severe wry nose

Contents

An Oldenburg colt with wry nose was autopsied after having lived for only 30 minutes. It presented cyanotic oral mucosae, underdeveloped eyes and a right-sided temporal osseous mass. The applicable nomenclature for the defects is discussed and the potential etiopathogenesis is explored by describing the normal embryonic development of the affected body parts.

Case history

A six-year-old Oldenburg mare, vaccinated against influenza, tetanus and rhinopneumonitis, was served by a BWP stallion. In the sixth gestational month, the primiparous mare was treated for pharyngitis with sulfadiazine-trimethoprim. Two weeks before the expected foaling date, a colt with wry nose and closed eyes was delivered (Fig. 1). It suffered from severe dyspnea and died within 30 minutes, after several attempts to stand up. The cadaver was grossly examined for didactical reasons at the University of Antwerp.

Gross findings

The rostral part of the *splanchnocranium* was deviated towards the left (Fig. 2), the palpebral fissures were only 5 mm in length, and the oral mucosae were slightly cyanotic. The body and extremities had the normal configuration. Systematic dissection of the various organ systems revealed that the lungs were inflated and the heart was cyanotic.

While preparing a didactical specimen of the skull, oval shaped orbits (4 cm in length and 2 cm in height) were noticed (Fig. 3). Each contained an undefined white mass embedded in fat and muscles. A rostral pigmented rim was suggestive for the iris. The ocular masses contained 4 mL of yellow liquid and a firm, opaque, spherical structure (5 mm in diameter) (Fig. 4). A solid mass (approximately 3 cm in diameter) was attached to the right temporal

crest. The brains that were harvested by removing the base of the skull appeared normal. Finally, the soft tissue remnants were macerated with sodium hypochlorite 42% (VWR International, Leuven, Belgium).

The maxillae, nasal bones and incisive bones were sigmoidally curved. A deviation of 110° in left caudolateral direction preceded a 40° deviation in rostro-ventral direction (Fig. 5). The nasal passages and *choanae* were obliterated (Fig. 6). The mandible was curved 25° to the left (Fig. 7). The temporal nodule was calcified and measured 3.2 cm (dorsoventral) by 2 cm (rostrocaudal) by 1.8 cm (mediolateral). A CT can of the skull using the Siemens Somatom-Emotion 6® scanner (München, Germany) revealed that two incisors with wide infundibula were implanted in an osseous cup (Fig. 8).

Discussion

The observed wry nose, wry mouth or *campylorrhinus lateralis* (Crowe and Swerczek 1985) is considered extreme because the deviation is over 90° and the mandible is additionally curved (Schumacher et al. 2008). Inability of the uterus to distend while the fetus grows and fusion of unilateral facial bones are potential etiologies (Vandeplassche et al. 1984; Dixon and Gerard 2012). Due to the absence of the contracted foal syndrome, extreme lack of intrauterine space cannot be substantiated in this case (Binanti et al. 2014). Other etiologies such as the ingestion of teratogenic plants, the administration of drugs and the exposure to infectious agents, insecticides and radiation have also been suggested (Pintore and Cantile 2015). Griseofulvin administration to a mare in the second gestational month and the subsequent birth of a foal with severe *brachygnathia superior* and *palatocheiloschisis* endorses this statement (Schutte and van den Ingh 1997). Indeed, the equine facial bones develop in the second gestational month (Rüsse, 1994). Neural crest cells first migrate from the caudal midbrain region and the first two hindbrain rhombomeres into the first pharyngeal

arch. This arch expresses OTX2 that is carried by the neural crest cells originating from the midbrain. The first pharyngeal arch thus responds to signals from the pouch endoderm by forming the maxilla and mandible (Sadler 2012). Based on this embryological time scale, the pharyngitis and treatment of the mare in the sixth gestational month seem unrelated to the wry nose.

The reason for not opening the eyes most probably lies in the presence of the small eyelids (*micropalpebrae)* and the reduced palpebral fissures and not in the potential prematurity of the foal. *Micropalpebrae* are pathognomonic for *microphthalmia* or *microphthalmos* and *nanophthalmos*. Since the eyes were not only small but also malformed, the former term is most appropriate to describe the underdeveloped eyes that were recessed in the orbits (*enophthalmos*) (Munroe and Barnett 1984). As for wry nose, toxic, mechanical, infectious and nutritional etiologies may have induced the bilateral *microphthalmia* when present at the time of embryonic eye development, i.e. between the 3rd and 5th gestational week (Munroe and Barnett 1984; Rüsse 1994). PAX6 initiates the cascade of gene expression that constitutes the single eye field (Zuber 2010). This is subsequently separated by SHH into two optic primordia from which optic vesicles are formed by the evagination of the neural ectoderm (Sadler 2012). One week later the optic cups and lens vesicles are formed from the invaginating optic vesicles and lens placodes, respectively (Rüsse, 1994; Sadler, 2012). Finally, optic fissure should be completed to generate adequate intraocular pressure allowing normal globe expansion that is required for the growth of multiple intraocular structures, such as the lens (Greenberg et al. 2015). The spherical structures found in the foal's eyes most probably represent underdeveloped lenses (*microphakia*) (Wilcock 1993).

Osseous masses at the base of the equine ear are known as temporal odontomes (Barker et al. 1993). The terms dysplasia or *hamartoma* are, however, more appropriate since they originate from the abnormal embryonic proliferation of normal tissues (Knowles et al.

2010). Our foal presented a compound *odontoma* since denticles, i.e. structures displaying features of normally developing teeth but lacking normal shape, were present (Andrews et al. 2014). In addition, the ectopic location of the teeth outside the dental arcades, which is the result of the aberrant migration of neural crest cells expressing HOX genes (Sadler 2012), justifies the term heterotopic *polyodontia* (Barker et al. 1993; de Mira et al., 2007). In the horse, tooth germ of the first branchial is commonly displaced with the first branchial cleft towards the ear or tympanic bulla due to genetic alterations, infections or external trauma (Dillehay 1986; Hidalgo-Sánchez et al. 2008). When the resulting ear or tympanic teeth (Barker et al. 1993; Miles and Grigson 2003) are located in a fistulating swelling, a dentigerous cyst is present (Dicht et al. 2011).

The simultaneous presence of *campylorrhinus lateralis*, bilateral *microphthalmia* and temporal *odontoma* in our foal (Fig. 9) cannot be attributed to the pharyngitis and the antibiotic treatment to which the mare was exposed in the sixth gestational month since the facial bones, eyes and teeth are formed four months earlier. As in 70% of birth defects, the etiology remains unknown (The Teratology Society, 2005). However, external trauma exerted by intrauterine malpositioning or lack of space cannot be excluded. Since the foal suffered from severe dyspnea and the nasal passages were completely obstructed, it most probably died from asphyxia.

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Conflict of interest

None declared.

References

Andrews C, Gadsen BJ, Carr EA, Kiupel M, 2014: Pathology in practice: Compound odontoma in a horse. JAVMA **244**, 417-419.

Barker IK, Van Dreumel AA, Palmer N, 1993: The alimentary system. In: Jubb KVF, Kennedy PC, Palmer N (eds), Pathology of domestic animals, 4th ed. vol. 2. Academic Press London, pp. 1-318.

Binanti D, Zani DD, De Zani D, Turci T, Zavaglia G, Riccaboni P, 2014: Contracted foal syndrome associated with multiple malformations in two foals. Anat Histol Embryol **43**, 71-74.

Crowe MW, Swerczek TW, 1985: Equine congenital defects. Am J Vet Res **46**, 353-358.

de Mira MC, Ragle CA, Gablehouse KB, Tucker RL, 2007: Endoscopic removal of a molariform supernumerary intranasal tooth (heterotopic polyodontia) in a horse. JAVMA **231**, 1374-1377.

Dicht S, Del Chicca F, Fürst A, 2011: Surgical removing of an ectopic tooth in an Iceland mare. Schweiz Arch Tierheilkd **153**, 569-572.

Dillehay DL, 1986: Complex odontoma in a horse. Vet Pathol **23**, 341-342.

Dixon P, Gerard M, 2012: Oral cavity and salivary glands. In: Auer J, Stick J (eds.), Equine surgery, 4th ed. Elsevier St Louis, pp. 339-367.

Greenberg SM, Plummer CE, Sledge D, Komine M, Craft SL, Conway JA, 2015: Bilateral microphthalmos with cyst in a neonatal foal. Vet Ophthalmol (in press).

Hidalgo-Sánchez O, Leco-Berrocal MI, Martínez-González JM, 2008: Metaanalysis of the epidemiology and clinical manifestations of odontomas. Med Oral Patol Oral Cir Bucal **13**, 730-734.

125 Knowles S, Blas-Machado U, Butler AM, Gomez-Ibañez SE, Lowder MQ, Fayrer-Hosken
126 RA, 2010: Ameloblastic fibro-odontoma associated with a retained molar in an
127 Oldenburg mare. J Vet Diagn Invest **22**, 987-990.
128 Miles AEW, Grigson C, 2003: Odontomes. In: Miles AEW, Grigson C (eds.), Colyer's
129 variations and diseases of the teeth of animals. Cambridge University Press, pp. 574-
130 606.
131 Munroe GA, Barnett KC, 1984: Congenital ocular disease in the foal. Vet Clin North Am
132 Large Anim Pract **6**, 519-537.
133 Pintore MD, Cantile C, 2015: Semilobar holoprosencephaly associated with multiple
134 malformations in a foal. Anat Histol Embryol (in press).
135 Rüsse I, 1994: Frühgravidität, Implantation und Plazentation. In: Rüsse I, Sinowatz F (eds.),
136 Lehrbuch der Embryologie der Haustiere. Blackwell Wissenschafts-Verlag Berlin-
137 Wien, pp. 153-246.
138 Sadler TW, 2012: Langman's medical embryology, 12th ed. Lippincott Williams & Wilkins
139 London.
140 Schumacher J, Brink P, Easley J, Pollock P, 2008: Surgical correction of wry nose in four
141 horses. Vet Surg **37**, 142-148.
142 Schutte JG, van den Ingh TSGAM, 1997: Microphthalmia, brachygnathia superior, and
143 palatocheiloschisis in a foal associated with griseofulvin administration to the mare
144 during pregnancy. Vet Quart **19**, 58-60.
145 The Teratology Society, 2005: Teratology Primer. http://www.teratology.org.
146 Vandeplassche M, Simoens P, Bouters R, De Vos N, Verschooten F, 1984: Aetiology and
147 pathogenesis of congenital torticollis and head scoliosis in the equine foetus. Equine
148 Vet J **16**, 419-424.

149 Wilcock BP, 1993: The eye and ear. In: Jubb KVF, Kennedy PC, Palmer N (eds), Pathology
150 of domestic animals, 4th ed. vol. 1. Academic Press London, pp. 441-529.
151 Zuber ME, 2010: Eye field specification in *Xenopus laevis*. Curr Top Dev Biol **93**, 29-60.
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Figure legends

Fig. 1: The living foal with wry nose.

Fig. 2: Left rostrolateral view of the head showing wry nose and the closed left eye.

Fig. 3: Left oval-shaped orbit after skinning the head. The underdeveloped eye shows a white, undefined mass with some pigmentation.

Fig. 4: Rostral view of the underdeveloped ocular structures. The pigmented rims (arrows) represent the underdeveloped iris.

Fig. 5: Left lateral view of the skull demonstrating the sigmoidally curved nose.

Fig. 6: Caudoventral view of the skull showing the obliterated *choanae* (arrows).

Fig. 7: Caudodorsal view of the deviated mandible.

Fig. 8: Right lateral (a) and caudal (b) views of the temporal *odontoma*. The radiodensity of the normotopic and ectopic teeth is similar (c). On a transverse CT-section the attachment of the *odontoma* to the temporal crest is visible (d).

Fig. 9: Three-dimensional reconstruction of the CT-scanned skull showing *campylorrhinus lateralis*, bilateral *microphthalmia* (characterized by the oval orbits) and temporal *odontoma*.

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Fig. 7

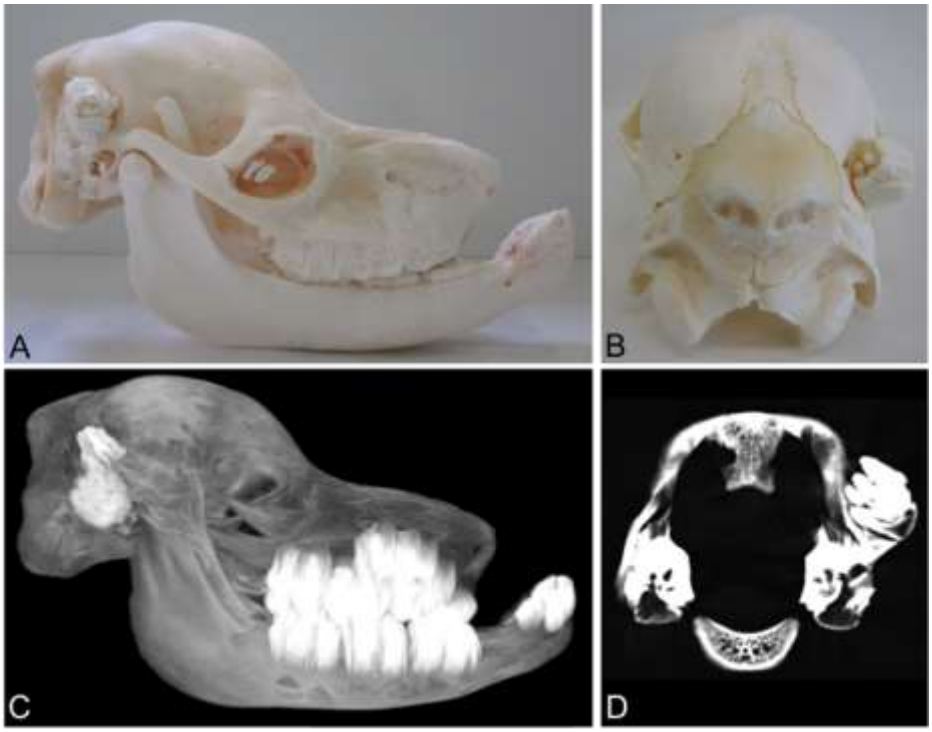

Fig. 8

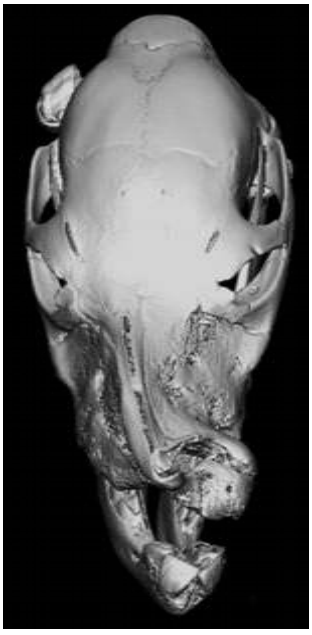

Fig. 9