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PITUITARY GLAND ABSCESS IN A HORSE SUBSEQUENT TO HEAD TRAUMA

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Summary

A 5-year-old thoroughbred gelding with recent history of head trauma presented with multiple facial swellings, bilateral mucopurulent nasal discharge, neck pain, inappetence and depression. On computed tomographic examination, lesions within the pituitary fossa and structures adjacent to the right guttural pouch were identified. Soft tissue swelling was seen in the dorsal aspect of the right guttural pouch surrounding several cranial nerves, with fluid-like material in the dependent portions of the right guttural pouch. The CSF sample contained mild mixed pleocytosis and increased protein level. The horse had concurrent periapical disease of the 209-cheek tooth and mild left sinusitis. The horse's demeanour deteriorated requiring euthanasia. Post mortem examination revealed a pituitary gland abscess.

Signalment, History and Clinical Findings

A 5-year-old thoroughbred gelding racehorse was presented to the Equine Referral Hospital, Royal Veterinary College (London, UK) for examination of facial swelling, bilateral nasal discharge, neck pain and inappetence. One month prior to presentation the horse had run into a fence causing a wound below the left eye. The wound was closed using skin sutures and responded well to antimicrobial treatment. Three weeks later, a left sided nasal discharge became evident; the horse was dull, ataxic on all four limbs, had multiple swellings over the head and was severely painful on neck flexion. There was a right-sided supraorbital swelling present, along with tenderness over the right guttural pouch region. Radiographic examination performed by the referring veterinary surgeon revealed fluid lines in the dependent part of the left conchofrontal and rostral maxillary sinuses. Upper airway endoscopy identified a swelling in the left guttural pouch consistent with an enlarged medial retropharyngeal lymph node. The horse was treated with further antimicrobials including 2.2mg/kg ceftiofur sodium SID IV (Excenel 50mg/ml, Zoetis UK Limited) and 10mg/kg oxytetracycline hydrochloride SID IV (Engemycin 10% (DD), MSD Animal Health, UK), alongside 4.4mg/kg phenylbutazone SID IV (Equipalazone 200mg/ml, Dechra Veterinary Products, UK) and one dose of 0.2mg/kg dexamethasone IV (Dexadreson 2mg/ml MSD Animal Health, UK) for three days but no improvement was seen and the horse was referred. Immediately prior to referral, swelling over the right guttural pouch had become more pronounced and extended to the area adjacent to the right temporomandibular joint (TMJ) and blood was obtained on aspiration. During repeat endoscopy, purulent material aspirated from the right

guttural pouch was submitted for culture and PCR, and found to be negative for *Strep. Equi. Equi*.

On admission to the hospital, the horse was quiet but responsive, in thin body condition (BCS 4/9) and had a bilateral serosanguinous nasal discharge. Four palpable swellings of the head were present; one was found in the right supraorbital fossa, a second was approximately 4cm in diameter, located ventral to the right TMJ and was firm and painful on palpation. A third, more diffuse swelling was positioned immediately caudal to the vertical ramus of the right mandible and was also painful on palpation. The fourth non-painful swelling was over the right nasoincisive notch. A focal area of erythema was present on the conjunctiva of the right eye, adjacent to the lateral canthus, and there was moderate blepharospasm and exophthalmos present alongside mild ventromedial strabismus. There was left masseter muscle atrophy and the horse masticated using the right dental arcades only. Clinical examination revealed symmetrical moderate to thin flat muscle covering over the cervical and dorsal thoracolumbar region. On physical exam, the horse had a stilted gait when circled to the left and when walked backwards, and the range of neck flexion was reduced bilaterally. The horse walked with the head and neck extended, however there were no signs of ataxia or paresis in any limb.

Imaging Diagnosis and Outcome

On the day of admission, the horse underwent standing computed tomographic of the head (CT) imaging using a 16-slice multi-detector CT scanner (GE Lightspeed Pro 16, GE Medical Systems, Berkshire, UK) using 120kV, 200mAs, 1.25mm slices

with an inter-slice interval of 1.25mm. Images were reconstructed using both a bone and soft tissue algorithm in a 512 x 512 matrix, and analysed by a board-certified radiologist (M.B) and a large animal radiology resident (R.E.M).

There was soft tissue attenuating material within the dependent portions of both the medial and lateral compartments of the right guttural pouch. The dorsal margin of this material had a convex appearance likely consistent with clotted blood or inspissated pus, perhaps secondary to infection of bacterial or fungal origin. There was also thickening of the soft tissue of the lateral wall of the lateral compartment of the right guttural pouch; most severe at the dorsal aspect. Soft tissue thickening was present in the dorsal aspect of the medial compartment of the right guttural pouch between the basisphenoid and the tympanic bulla; the swelling was in close relationship with the jugular foramen and cranial nerves IX, X and XI (glossopharyngeal, vagus and accessory, respectively; Figure 1). The pituitary gland measured 1.9 x 2.4 x 3.7cm (dorsoventral height, laterolateral width and rostrocaudal length, respectively), which is slightly larger than the sizes published for clinically normal horses (Crijns et al. 2017, Luedke et al. 2017). A focal area of hyperattenuation, likely consistent with mineralisation, was present in the caudal aspect of the gland, immediately left of midline (Figure 2). Differential diagnoses for the pituitary lesion included normal age-related changes in size (Crijns et al. 2017), melanotrope hyperplasia and macroadenoma formation in the pituitary pars intermedia (McFarlane 2011, Kolk et al. 2004) as most likely differentials; other differential diagnoses such as infectious or inflammatory process of the pituitary gland (abscessation, pituitary hypophysitis), or cystic echinococcus (*Echinococcus equinus*) were considered less

likely. There was no evidence of masseter muscle atrophy or exophthalmos on the CT examination.

The periapical space of 209 was widened and gas attenuation was present within the apex of the palatal mesial pulp horn of 209, which communicated with the rostro-palatal aspect of the periapical space. Adjacent to this, there was a small (4 x 4 x 4mm) round mineral attenuating body, consistent with a cementoblastoma (Luedke et al. 2017). Fluid/soft tissue attenuating material was present within the dependent aspect of the left rostral maxillary sinus, the rostral aspect of the left caudal maxillary sinus and the dependent aspect of left conchofrontal sinus. Rostrally, the ventral nasal conchal bulla wall was distorted, compressed and thickened. Imaging findings were consistent with periapical infection of 209 and secondary sinusitis. These were likely chronic and unrelated to the recent clinical history.

Guttural pouch endoscopy was performed under standing sedation and confirmed the CT findings. The soft tissue thickening in the dorsomedial aspect of the right guttural pouch was identified and when pressure was applied by the endoscope, mucopurulent fluid drained from this swelling into the guttural pouch; this was aspirated and submitted for culture and sensitivity. Ultrasonographic examination of the swelling ventral to the right TMJ was carried out using a GE Logiq E9 ultrasound machine and linear transducer with a frequency of 10-14mHz. A well-encapsulated area of heterogeneous echogenicity, consistent with an abscess, was situated within the medial aspect of the right masseter muscle (Figure 3). Aspiration of this mass revealed a turbid gelatinous fluid containing

126 >99% degenerate neutrophils consistent with septic neutrophilic inflammation.
127 The other abscesses were not evaluated using ultrasonography. On culture of the
128 fluid profuse *micrococcus* species was identified. Similar microbes were harvested
129 from the right guttural pouch sample collected during endoscopy, with a broad
130 sensitivity. The horse was also suffering from a thrombosed jugular vein and
131 tributaries, confirmed during ultrasonographic examination.
132
133 Biochemistry results, collected on two occasions; when the horse was admitted
134 and 3 days later, revealed an elevated total protein (74.9g/l; ref range 50-64 g/l)
135 and globulin (48.1; ref range 16-30g/l), and a decreased creatinine (102; ref range
136 121-194umol/l), albumin (26.8; ref range 31-38g/l), aspartate aminotransferase
137 (AST) (100; ref range 198 – 476U/l) and creatinine kinase (CK) (59; ref range 133
138 – 738U/l). The horse was administered 8mg/kg oxytetracycline (Engemycin 10%,
139 MSD Animal Health, UK) SID IV and 1.1mg/kg flunixin meglumine (Meflosyl 5%,
140 Zoetis, USA) BID IV for 48 hours over which time the horse's demeanour waxed
141 and waned. On re-examination using guttural pouch endoscopy and
142 ultrasonography, the abscess appeared to be draining into the guttural pouch and
143 reducing in size.
144
145 Despite the antimicrobial, NSAID and intravenous fluid therapy, the horse's
146 demeanour became consistently dull. Cerebrospinal fluid (CSF) was sampled
147 using a lumbosacral approach and cytological analysis revealed a mild mixed
148 pleocytosis with lymphocyte dominance (12% non-degenerate neutrophils, 46%
149 lymphocytes, 10% granular lymphocytes, 1% monocytes and 1% vacuolated
150 macrophages). This fluid also had an increased total protein of 1.4g/l, consistent

with either inflammation or blood contamination. A local or general response to an infectious or inflammatory process may explain these findings. The horse was eventually euthanised due to a deterioration over a two-week period.

Post-mortem Examination

Within the brain, a multi-nodular, variably soft to firm, partially cavitated mass was observed in the region of the pituitary gland. On microscopic examination parts of the anterior pituitary gland and trigeminal nerve were surrounded and displaced by fibrin aggregates, admixed with bacterial colonies, cellular debris (necrosis) and large numbers of viable and degenerate neutrophils. Reactive fibroblasts, mature collagen and large macrophages that occasionally contained golden brown granular pigment (haemosiderophages) surrounded these structures. This is likely consistent with a chronic abscess with intra-lesional bacterial colonies. Culture of these colonies from direct and enriched culture revealed *Enterococcus faecalis, Coliform* and *Bacteroides* species. No further abnormalities were detected within the brain.

Firm multifocal inspissated masses, measuring 3 x 3 x 3cm, were found throughout the pterygoid muscles, and parotid and mandibular salivary glands adjacent to the lateral aspect of the right guttural pouch, also likely consistent with abscessation of a similar nature to the pituitary gland. The mandibular salivary gland had evidence of vasculitis, thrombosis and haemorrhage. Although bacterial colonies were not visualised in the mandibular salivary gland, the abundance of viable and degenerate neutrophils detected, alongside a mixed bacterial growth, was most consistent with a septic lesion. Culture of the abscess within the lateral

right guttural pouch revealed a moderate growth of *Coliform* species from direct culture, and *Staphylococcus aureus* and *Bacteroides* spp from enrichment culture.

Discussion

This horse presented with two disease processes occurring concurrently. The primary problem was the infectious processes affecting the pituitary region, cranial nerve neuritis, right guttural pouch empyema and multifocal abscessation. The second was periapical disease affecting the 209 tooth and causing secondary left-sided sinusitis.

The pituitary mass was considered in this case, the limiting factor for the horse's recovery. The most likely differential diagnoses for enlargement of the pituitary gland in the horse, seen on CT images, are either normal age-related changes or melanotrope hyperplasia and macroadenoma formation in the pituitary pars intermedia (Pease et al. 2011). Normal measurements of the pituitary gland on CT have been reported to range from approximately 2.0–2.2cm rostrocaudal length, 1.8-2.16cm laterolateral width, and 0.98-1.4cm dorsoventral height (Crijns et al. 2016, Kolk et al. 2004, McKlveen et al. 2003), with those suffering from pituitary pars-intermedia dysfunction (PPID) measuring on average 2.6±0.3cm rostrocaudal length, 2.4±0.26cm laterolateral width, and 1.92±0.43cm dorsoventral height (Kolk et al. 2004). Enlarged pituitary glands can also be found in horses with no neurological signs and without PPID. Pituitary gland size can increase proportionally with the age and weight of the horse, and the gland can also undergo disproportionate growth (grade 2 PPID) as the pars-intermedia hypertrophies due to normal age-related changes without subsequent increases

in plasma ACTH levels (Crijns et al. 2017). This explanation provided the most likely differential diagnosis in this case. However, in retrospect, the presence of mineralization within the mass is an unusual finding for normal age-related changes of the pituitary gland, and it may indicate that abscessation was more likely. The use of intravenous contrast medium could have been helpful, especially due to the cavitary nature of the lesion, however, because of financial constraints this was not performed. The histopathological findings and culture of intra-lesional bacterial colonies confirmed that this lesion was an abscess. The presence of surrounding granulation tissue and fibrosis were consistent with the chronic four-week history. The source of bacterial infection could either be due to direct inoculation from a nearby structure, such as chronic guttural pouch empyema or less likely because of extension of the tooth root abscess or sinusitis (Smith et al. 2004), or haematogenous spread (Reilly et al. 1994). With a history of previous head trauma and subsequent right-sided facial swellings, it is likely that there was an association between these factors; the trauma may have caused several haematomas including one within the guttural pouch which subsequently became infected. Infection may then have spread via the guttural pouch into the adjacent dorsal soft tissues structures, through the jugular foramen into the meninges, myelencephalon and propagated rostrally to the pituitary gland. However, the horse also had systemic signs of an inflammatory response and meningitis, therefore haematogenous spread of infection is possible. Haematogenous spread was the cause of pituitary abscesses in cattle, in several reports (Perdrizet and Dinsmore 1986, Braun et al. 2017). In a case series of 7 horses, brain abscesses (including 4 pituitary abscesses) were thought to spread from the sinuses, nasal cavity, periocular tissues or submandibular lymph nodes (Smith et al. 2004). In

another report of four horses with pituitary abscesses, a site of infection near the pituitary fossa (sphenopalatine sinus in 2 horses and the guttural pouch in 1 horse) was identified and hypothesised to be the source of infection (Reilly et al. 1994). Clinical signs such as anorexia, depression, recumbency and ataxia were recorded in a case series of four horses that suffered from pituitary abscesses (Reilly et al. 1994). Depression and inappetence were also observed in this horse. The pituitary gland is responsible for producing a range of hormones including growth hormones, reproductive hormones, adrenocorticotropic hormone (ACTH), oxytocin and antidiuretic hormone (ADH). Hypoadrenocorticism can lead to depression, a lack of appetite and paresis, which may have occurred in this patient due to destruction of the pituitary gland.

Left sided masseter muscle atrophy and lack of left sided mastication were detected during the clinical examination, however masseter muscle atrophy was not detected on the CT examination. There was no evidence of dysphagia and it is more likely that the lack of appetite was associated with the pituitary lesion and systemic inflammation and/or the left sided periapical dental disease. It is unusual that there was little manifestation of cranial nerve deficits in this case, especially when compared to a similar case describing a pituitary abscess in a bull, in which a lack of tongue tone, jaw tone, dysphagia, salivation, a head tilt to the right and unilateral ptosis were observed (Braun et al. 2017). Conjunctival hyperaemia, causing erythema, can be observed with Horner's syndrome due to the interruption of sympathetic innervation causing vessels to vasodilate (Furr and Reed 2015). In this case the cranial cervical ganglion (part of the sympathetic

tract) located in the wall of the guttural pouch may have been affected, subsequently causing the conjunctival erythema seen.

In conclusion, this horse likely suffered abscessation of the pituitary gland as a result of extension of a guttural pouch infection or haematogenous spread. Although this is an unusual condition, it should be considered in horses that remain dull after head trauma, and if focal mineralization is found in a mass on CT. The recent history of head trauma makes it likely that this was the result of trauma.

List of Author Contributions

(a) Conception and Study Design: R. E. Morgan, M. Biggi

(b) Acquisition of Data: R. E. Morgan, M. Biggi, A. R. Fiske-Jackson

(c) Data analysis and Interpretation: R. E. Morgan, M. Biggi

(d) Preparation of the manuscript: R. E. Morgan, M. Biggi

(e) Revising Article for Intellectual Content: R. E. Morgan, M. Biggi, A. R. Fiske-Jackson

(f) Final Approval of the Manuscript: R. E. Morgan, M. Biggi, A. R. Fiske-Jackson

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Conflict of Interest

There are no conflicts of interest.

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I.

Figure 1. Transverse bone algorithm (window length 300, window width 1500) computed tomography (CT) image at the level of the jugular foramen (jugular f.) through which cranial nerves IX, X and XI exit the skull. The right side of the horse's head is on the left side of the image. The soft tissues surrounding the right foramen (arrowheads) are thicker than the contralateral side, and there is soft tissue attenuating material within the dependent aspect of the right guttural pouch (arrows).

II.

Figure 2. A, Sagittal and B, Transverse brain algorithm (window length 50, window width 100) computed tomography images at the level of the pituitary fossa. In B, the right side of the horse's head is on the left side of the image. The pituitary lesion is highlighted by the arrowheads. An area of hyperattenuation, consistent with mineral attenuation, is present within the left side of the pituitary fossa (arrows). The soft tissues of the dorsal and lateral aspects of the right guttural pouch are also thickened (block arrows).

III.

Figure 3. Ultrasound image of the swelling situated ventral to the right temporomandibular joint. A well-encapsulated area of mixed echogenicity can be seen (arrowheads), likely consistent with an abscess within the right masseter muscle.