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1 **PITUITARY GLAND ABSCESS IN A HORSE SUBSEQUENT TO HEAD TRAUMA**

2

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11

12 **Key words: horse, pituitary, abscess, trauma, head**

13

14 **Summary**

15 A 5-year-old thoroughbred gelding with recent history of head trauma presented

16 with multiple facial swellings, bilateral mucopurulent nasal discharge, neck pain,

17 inappetence and depression. On computed tomographic examination, lesions

18 within the pituitary fossa and structures adjacent to the right guttural pouch were

19 identified. Soft tissue swelling was seen in the dorsal aspect of the right guttural

20 pouch surrounding several cranial nerves, with fluid-like material in the

21 dependent portions of the right guttural pouch. The CSF sample contained mild

22 mixed pleocytosis and increased protein level. The horse had concurrent

23 periapical disease of the 209-cheek tooth and mild left sinusitis. The horse's

24 demeanour deteriorated requiring euthanasia. Post mortem examination

25 revealed a pituitary gland abscess.

26

27 **Signalment, History and Clinical Findings**

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

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

53

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

71

72 **Imaging Diagnosis and Outcome**

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

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

79

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

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

103

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

115

116 Guttural pouch endoscopy was performed under standing sedation and confirmed
117 the CT findings. The soft tissue thickening in the dorsomedial aspect of the right
118 guttural pouch was identified and when pressure was applied by the endoscope,
119 mucopurulent fluid drained from this swelling into the guttural pouch; this was
120 aspirated and submitted for culture and sensitivity. Ultrasonographic
121 examination of the swelling ventral to the right TMJ was carried out using a GE
122 Logiq E9 ultrasound machine and linear transducer with a frequency of 10-
123 14mHz. A well-encapsulated area of heterogeneous echogenicity, consistent with
124 an abscess, was situated within the medial aspect of the right masseter muscle
125 (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

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

154

155 **Post-mortem Examination**

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

167

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

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

178

179 **Discussion**

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

185

186 The pituitary mass was considered in this case, the limiting factor for the horse's
187 recovery. The most likely differential diagnoses for enlargement of the pituitary
188 gland in the horse, seen on CT images, are either normal age-related changes or
189 melanotrope hyperplasia and macroadenoma formation in the pituitary pars
190 intermedia (Pease et al. 2011). Normal measurements of the pituitary gland on CT
191 have been reported to range from approximately 2.0–2.2cm rostrocaudal length,
192 1.8-2.16cm laterolateral width, and 0.98-1.4cm dorsoventral height (Crijs et al.
193 2016, Kolk et al. 2004, McKlveen et al. 2003), with those suffering from pituitary
194 pars-intermedia dysfunction (PPID) measuring on average 2.6 ± 0.3 cm
195 rostrocaudal length, 2.4 ± 0.26 cm laterolateral width, and 1.92 ± 0.43 cm
196 dorsoventral height (Kolk et al. 2004). Enlarged pituitary glands can also be found
197 in horses with no neurological signs and without PPID. Pituitary gland size can
198 increase proportionally with the age and weight of the horse, and the gland can
199 also undergo disproportionate growth (grade 2 PPID) as the pars-intermedia
200 hypertrophies due to normal age-related changes without subsequent increases

201 in plasma ACTH levels (Crijns et al. 2017). This explanation provided the most
202 likely differential diagnosis in this case. However, in retrospect, the presence of
203 mineralization within the mass is an unusual finding for normal age-related
204 changes of the pituitary gland, and it may indicate that abscessation was more
205 likely. The use of intravenous contrast medium could have been helpful, especially
206 due to the cavitory nature of the lesion, however, because of financial constraints
207 this was not performed. The histopathological findings and culture of intra-
208 lesional bacterial colonies confirmed that this lesion was an abscess. The presence
209 of surrounding granulation tissue and fibrosis were consistent with the chronic
210 four-week history. The source of bacterial infection could either be due to direct
211 inoculation from a nearby structure, such as chronic guttural pouch empyema or
212 less likely because of extension of the tooth root abscess or sinusitis (Smith et al.
213 2004), or haematogenous spread (Reilly et al. 1994). With a history of previous
214 head trauma and subsequent right-sided facial swellings, it is likely that there was
215 an association between these factors; the trauma may have caused several
216 haematomas including one within the guttural pouch which subsequently became
217 infected. Infection may then have spread via the guttural pouch into the adjacent
218 dorsal soft tissues structures, through the jugular foramen into the meninges,
219 myelencephalon and propagated rostrally to the pituitary gland. However, the
220 horse also had systemic signs of an inflammatory response and meningitis,
221 therefore haematogenous spread of infection is possible. Haematogenous spread
222 was the cause of pituitary abscesses in cattle, in several reports (Perdrizet and
223 Dinsmore 1986, Braun et al. 2017). In a case series of 7 horses, brain abscesses
224 (including 4 pituitary abscesses) were thought to spread from the sinuses, nasal
225 cavity, periocular tissues or submandibular lymph nodes (Smith et al. 2004). In

226 another report of four horses with pituitary abscesses, a site of infection near the
227 pituitary fossa (sphenopalatine sinus in 2 horses and the guttural pouch in 1
228 horse) was identified and hypothesised to be the source of infection (Reilly et al.
229 1994). Clinical signs such as anorexia, depression, recumbency and ataxia were
230 recorded in a case series of four horses that suffered from pituitary abscesses
231 (Reilly et al. 1994). Depression and inappetence were also observed in this horse.
232 The pituitary gland is responsible for producing a range of hormones including
233 growth hormones, reproductive hormones, adrenocorticotrophic hormone
234 (ACTH), oxytocin and antidiuretic hormone (ADH). Hypoadrenocorticism can lead
235 to depression, a lack of appetite and paresis, which may have occurred in this
236 patient due to destruction of the pituitary gland.

237

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

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

252

253 In conclusion, this horse likely suffered abscessation of the pituitary gland as a
254 result of extension of a guttural pouch infection or haematogenous spread.

255 Although this is an unusual condition, it should be considered in horses that
256 remain dull after head trauma, and if focal mineralization is found in a mass on CT.

257 The recent history of head trauma makes it likely that this was the result of
258 trauma.

259

260 **List of Author Contributions**

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

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

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

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

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

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

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272 **Conflict of Interest**

273 There are no conflicts of interest.

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276

277 **References**

278

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339 I.

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

347 II.

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

355 III.

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