Imaging characteristics of a multifocal choroid plexus carcinoma with bilateral calvarial defects in a dog

Authors:

Jonathan R. Hughes[1], Frances E. Taylor-Brown[2], Oliver Greville-Heygate[1], Fernando Constantino-Casas[1], David L. Williams[1], Marie-Aude Genain[1].

[1] Queen's Veterinary School Hospital, Madingley Rd, Cambridge, CB3 0ES.

[2]Cave Veterinary Specialists, George's Farm, West Buckland, TA21 9LE

Correspondence: Jonathan Hughes, Queen's Veterinary School Hospital, Madingley Rd, Cambridge, CB3 0ES. jrh216@cam.ac.uk.

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Abstract:

An 8-year-old male intact miniature poodle presented for blindness, obtundation, tetraparesis and vestibular signs. Magnetic resonance imaging (MRI), radiography and ultrasound revealed a left piriform lobe lesion, right cerebellar and left brainstem lesions, hydrocephalus and bilateral calvarial defects. Histopathology confirmed a choroid plexus carcinoma with meningeal and intraventricular metastases. The calvarial defect did not show evidence of necrosis, osteoclastic resorption, inflammation or neoplastic infiltration, reflecting a quiescent calvarial atrophy or dysplasia. The imaging characteristics are indicative of calvarial atrophy secondary to chronic increased intracranial pressure and this is the first report of a calvarial defect of this size.

Signalment, History, Clinical Findings

An 8-year old male intact miniature poodle (body weight – 6kg) presented with a history of progressive blindness, behaviour change and an abnormal gait. Neurological examination revealed mild obtundation, a left-sided head tilt with right-sided hypermetria and vestibulocerebellar ataxia. There were absent menace responses bilaterally, mydriasis, left positional ventrolateral strabismus and marked cervical and lumbar hyperaesthesia. Neuroanatomical localisation was consistent with a multifocal brain lesion – forebrain, right cerebellum, brainstem and the spinal cord. The dog was mildly anaemic (haematocrit 31.6%; 37-55), but otherwise haematology, biochemistry and urinalysis were unremarkable.

Imaging, Diagnosis and Outcome

MRI of the brain was performed in sternal recumbency in a 0.3 Tesla MRI unit (Esaote, VetMR, Via Siffredi, Genoa, Italy) with the ankle coil . Transverse and sagittal plane T2-weighted (TR 5500-7200ms, TE 90ms, slice thickness 3-3.5mm, interval 0.33-0.39mm); transverse, sagittal and dorsal T1-weighted (TR 350-450ms, TE 26ms, slice thickness 3-3.5mm, interval 0.33-0.39mm); transverse FLAIR (TR 7260ms, TE 90ms, TI 1800, slice thickness 3mm, interval 0.33mm) and T2*-weighted (TR 1200ms, TE 22ms, flip angle 40, slice thickness 3mm, interval 0.38mm) and post contrast T1-weighted (Gadolinium, Gadovist, Bayer Inc, Mississauga, Ontario, Canada, 0.1 ml/kg) sequences were included.

Centred on the left piriform lobe, there was a poorly defined, focal, heterogeneous, T2-weighted and FLAIR hyperintense, T1-weighted isointense to grey matter lesion with moderate contrast enhancement, (Fig. 1) which had multifocal T2-weighted hyperintense, FLAIR suppressing foci suggestive of a cystic component. The lesion was causing left sided

compression of the pons and midline shift of the brainstem. Adjacent to and associated with the caudal aspect of the left medulla oblongata and in the right cerebellum, there were multifocal, well-demarcated lesions of similar signal intensity to the piriform lesion.

The left cerebral white matter, cerebellum, thalamus and brainstem were diffusely T2-weighted and FLAIR hyperintense, consistent with vasogenic oedema. There was diffuse ventriculomegaly, piriform lobe atrophy and FLAIR hyperintensity of the ventricular lining (interstitial oedema). The lining of the third ventricle and meninges surrounding the rostral colliculi were contrast enhancing. Increased intracranial pressure was suspected due to the mass effect, oedema, small interthalamic adhesion and effacement of the cerebral sulci.[1]

There was loss of the T1-weighted hypointense calvarial bone signal bilateral to the cerebrum, larger on the left, leaving a dorsal cap of residual bone with irregular edges and multifocal regions of thinning, away from the defect margins (Fig. 2). The cerebrum bulged laterally and was in contact with the temporal muscles. There was linear contrast enhancement of the temporal muscles adjacent to the dura and overlying the residual calvarial bone, most prominently overlying the left dorsolateral edge.

Skull radiographs (AGFA CRMD 4.0, AGFA CR85-X, lateral view and ventrodorsal, kV 50, mAs 6.4) showed loss of the normal convolutional skull markings of the lateral skull, leaving a large irregular defect replaced by homogeneous soft tissue opacity and a dorsal calvarial cap (Fig. 3A).

On ultrasound (Phillips EPIQ 7, Linear 12-5MHz, Philips UK Ltd), the brain was visible from the lateral aspects of the head confirming the absence of bone separating the meninges from the surrounding peri-calvarial soft tissues. The brain parenchyma was mainly homogeneously hypoechoic to the superficial soft tissues with poorly defined hyperechoic

regions and a thin hyperechoic meningeal lining. The sulci of the cerebellum were prominent but minimal cerebral sulci were visible (Fig. 3B and C).

Overall, the imaging examinations documented multifocal brain lesions likely originating from the fourth ventricle and spread via the ventricular and meningeal pathways. An extra-axial central nervous system (CNS) neoplasia with metastases (choroid plexus tumour, ependymoma) was most likely. Due to the parenchymal involvement, a gliomatosis or disseminated haemangiosarcoma, lymphoma or histiocytic sarcoma were considered.[2] Inflammatory, infectious or degenerative lesions were less likely. The bilateral asymmetrical calvarial defects and small dispersed areas of thinning were suggestive of neoplastic invasion, necrosis or atrophy due to chronic raised intracranial pressure. Calvarial dysplasia was considered unlikely from the imaging characteristics.

The dog recovered from anaesthesia but was more obtunded post anaesthetic with an intermittent decerebellate posture and was euthanised after 48 hours of increasing dyspnoea.

On gross post-mortem, there was an approximately 50x45mm bilateral calvarial defect with irregular margins in the parietal bone, but including the caudal frontal, dorsal temporal and rostral occipital bones. The defect was covered by skin, skeletal muscle and a smooth, cream-coloured deep layer. The remaining calvarium exhibited multifocal areas of thinning (2-5mm; Fig. 4B and C).

The brain was enlarged and bulging through the bilateral defects. On cut surface, there was a focal, well-demarcated, tan, soft, irregular, granular mass (approximately 10x10mm) in the left piriform lobe. A similar lesion was seen lining the longitudinal fissure

and fourth ventricle. There was diffuse, moderate, ventricular enlargement (non-communicating hydrocephalus).

The tissue overlying the calvarial defect was composed of skeletal muscle and thin anastomosing trabeculae of woven bone and a loose fibrovascular stroma, bordered by bundles of mesenchymal cells (Fig. 4A). No osteoclasts or signs of bone resorption were visible. There was no compact bone. The adjacent skeletal muscle was multifocally infiltrated by lymphocytes and fewer plasma cells (myositis).

The left piriform lobe was infiltrated by a large, unencapsulated neoplastic mass histologically consistent with a choroid plexus carcinoma (CPC). Neoplastic cells were arranged in papillae supported by a branching, fibrovascular stroma. Individual cells were indistinct, cuboidal to columnar with moderately eosinophilic cytoplasm. There were <1 mitoses per 10 high power fields. There was mild anisocytosis and moderate anisokaryosis. Rare strands of eosinophilic material admixed with karyorrhectic debris (necrosis) between the papillae were seen. Corresponding neoplastic infiltrations were present in the longitudinal fissure, third and fourth ventricles and infiltrating the grey matter of the cingulate gyri and cerebellar cortex bilaterally and the left medulla oblongata.

Histopathology of the lung was consistent with subacute, focal, moderate, neutrophilic, histiocytic bronchopneumonia of the right cranial and middle lobes.

Discussion

Choroid plexus tumours are a well-documented primary CNS neoplasm in the dog and account for 7-10% of all primary intracranial CNS neoplasia. [2,3] Their MRI characteristics are well described.[2-5] The MRI, radiographic and ultrasound findings and correlating histopathology showed multifocal lesions in the left piriform lobe, right cerebellum and left medulla oblongata likely originating from the fourth ventricle and metastases via the subarachnoid space and ventricles, consistent with previously described CPC's and meningeal carcinomatosis.[6,7] In dogs, CPC's make up around 60% of choroid plexus tumours, 53% of which were found to have metastases on post-mortem but only 35% of these were visible on MRI.[3] Therefore, these metastatic imaging characteristics are rarely reported for CPC's. In humans, approximately 12% of patients diagnosed with CPC's present with metastases.[7]

To the authors' knowledge, there are no previous reports of canine calvarial defects to this extent, characterised with both MRI and radiography and allowing transcutaneous ultrasound of the brain. More commonly hyperostosis has been described with intracranial neoplasia, particularly with meningiomas. [6,8,9] No evidence of lysis, osteoclastic resorption, inflammation or neoplastic infiltration were seen and the defects were bilateral and extensive. The histopathological appearance of this tissue cannot definitively differentiate between chronic atrophy and dysplasia.

The spatial resolution and detail of bone is not optimal on low-field MRI and it is difficult to differentiate benign and aggressive bone lesions. Radiography better characterised the sharpness of the defect margins and better assessed the remaining calvarium for lytic lesions. The smooth lateral defect margins were suggestive of a chronic atrophy rather than infiltrative destruction. Ultrasound was performed to assess for the

presence of meninges, for thin residual mineralisation between the dura and temporal muscles not seen on MRI and detection of safely sampleable lesions, whether intracranial or corresponding to the muscular contrast enhancement. The focal muscular contrast enhancing lesion was not visualised with ultrasound and intracranial lesions were not safely sampleable.

The asymmetrical, dispersed small sites of thinning of the inner cortex and absent diploe of the calvarium suggest the causative process was intracranial. The defect was larger on the ipsilateral side to the suspected primary lesion and the transition zone was irregular and asymmetrical (Fig. 2). The calvarial thinning could be explained by a chronic increase in pressure exerted around the piriform lobes. This has been described in humans, but not specifically in relation to CPC. [10] Neoplasms release matrix metalloproteinases (MMP's) that cause degradation of bone extracellular matrices. This has been a suggested mechanism of calvarial loss in meningiomas,[11] and could explain the diffuse atrophy given the meningeal metastases. MMP-9 has been shown to be detectable in dogs with choroid plexus tumours compared to those without.[12] The cause of the myositis was unclear, however pressure from cerebral swelling and physical trauma could be considered.

Calvarial atrophy has been previously reported with a canine glioma but not with CPC.[6] In the glioma case, the defect was similarly characterised by thinning, alteration of the bone and a residual collagen layer.[6] The MR features and histopathology of the brain lesion in this patient have been previously similarly reported, but the MR or radiographic features of the calvarium were not described.[13]

Diffuse skull thinning in humans can be a result of chronic hydrocephalus or congenital malformations and focal thinning due to underlying neoplasia. [13] CPC's are often

found in children (median age of 3 years old), although calvarial atrophy has not been reported.[7]

To the authors' knowledge, this is the first report of suspected acquired calvarial defects of this size associated with intracranial neoplasia without evidence of invasion, inflammation, necrosis or osteoclastic resorption. The extent of the calvarial defect was not only unique but should be considered as a sequela of raised intracranial pressure due to CPC with meningeal metastases even in the presence of a quiescent process on histopathology.

AUTHOR CONTRIBUTIONS

Category 1

(a) Conception and design: Jonathan Hughes, Marie-Aude Genain

(b) Acquisition of data: Jonathan Hughes, Frances Taylor-Brown, Oliver Greville-Heygate, Fernando Constantino-Casas, David Williams, Marie-Aude Genain

(c) Analysis and interpretation of data: Jonathan Hughes, Frances Taylor-Brown, Oliver Greville-Heygate, Fernando Constantino-Casas, David Williams, Marie-Aude Genain

Category 2

(a) Drafting the article: Jonathan Hughes

(b) Revising the article: Jonathan Hughes, Frances Taylor-Brown, Oliver Greville-Heygate, Fernando Constantino-Casas, David Williams, Marie-Aude Genain

Category 3

(a) Final Approval: Jonathan Hughes, Frances Taylor-Brown, Oliver Greville-Heygate, Fernando Constantino-Casas, David Williams, Marie-Aude Genain

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Figure Legend

Figure 1. MRI of the brain of the dog. (A) Transverse T2w (B) T1w post-contrast (C) FLAIR images. Poorly defined heterogeneous lesion of mixed intensity and contrast enhancement in the left piriform lobe (arrows). Absent calvarial bone overlying the piriform lobes and residual cap of calvarium (arrowhead). (D) Corresponding transverse gross post mortem section of the brain at the level of the lesion.

Figure 2. MRI of the brain of the dog. (A) Transverse and (B) dorsal planes showing the bilateral, asymmetrical loss of calvarium (arrowheads) and multifocal thinning away from the margin (arrow) compared to a normal calvarium (C and D).

Figure 3. (A) Lateral skull radiograph. Loss of normal calvarial convolutional markings laterally with irregular margins. (B)Ultrasound images (Linear 12-5MHz) of the cerebrum with poorly defined cerebral sulci. (C) Ultrasound images (Linear 12-5MHz) of the cerebrum and cerebellum containing poorly defined hyperechoic regions, lined by a hyperechoic rim.

Figure 4. (A) Haematoxylin and Eosin stain, 100x magnification, Photomicrograph of the trabeculae of woven bone (arrow) supported by a loose fibrovascular stroma. Bundles of spindle cells (arrowhead) between bony trabeculae. (B) 10x magnification, Single layer of compact bone from a section of intact frontal bone, exhibiting multifocal areas of thinning (arrows) and absent diploe. (C) Gross post mortem image of the frontal bone demonstrating multifocal areas of thinning (arrows).