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CASE REPORT

Companion or pet animals

# Papillary meningioma with multifocal leptomeningeal spread in a dog

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This case report was presented at the British Veterinary Neurology Society (BVNS) symposium 2021.

**Abstract**

An 11-year-old, English cocker spaniel was presented with subacute progressive signs of vestibular ataxia, tetraparesis, left-sided proprioceptive deficits, positional ventrolateral strabismus of the right eye and a right-sided menace deficit. Magnetic resonance imaging of the cranium and cranial cervical spinal cord revealed multifocal T2 hyper-/T1-hypointense intradural lesions with dural tail signs and intra-axial and intramedullary extension. Medical treatment resulted in initial improvement before deterioration was noticed. Cytological examination results of computed tomography-guided fine-needle aspiration biopsy of the C1–C2 lesion were consistent with mesenchymal neoplasia. Three days later, after progressive clinical deterioration, euthanasia was performed. Postmortem examination and subsequent histological examination of the brainstem and spinal cord revealed multifocal, strongly infiltrative growth of neoplastic cells with areas of pseudo-rosette formation by cylindrical neoplastic cells with moderately large, oval nuclei in addition to areas of spindle-shaped neoplastic cells with meningothelial whorls. The final diagnosis was a papillary (grade III) meningioma with multifocal leptomeningeal spread.

**KEYWORDS**

brain diseases, leptomeningeal metastasis, neoplasia, pseudorosettes

## BACKGROUND

Meningioma is the most common primary brain tumour in dogs and cats.[1] Due to similarities between canine and human meningiomas, the WHO histological classification system is commonly applied.[2–5] Meningiomas are categorised as grade I, II or III, in increasing order of malignancy. One of the histological subtypes, papillary meningioma (PM), is classified as grade III in the human classification system, due to a tendency for invasion of the brain, local recurrence after removal and metastasis. This case report describes clinical, imaging and histological findings of PM with rarely described multifocal leptomeningeal spread (intracranial and spinal) in a dog.

## CASE PRESENTATION

An 11-year-old, female, neutered English cocker spaniel was presented with subacute progressive neurological signs of vestibular ataxia. General examination was unremarkable. Neurological examination revealed vestibular ataxia with a left-sided head tilt, tetraparesis, left-sided proprioceptive deficits, positional ventrolateral strabismus of the right eye and right-sided menace deficits. There were no signs of pain on palpation of the head and vertebral column. Other parts of the neurological examination were unremarkable. The anatomical neurolocalisation was multifocal intracranial, possibly including the cervical spinal cord, at least with involvement of central vestibular systems based on the vestibular ataxia, head tilt and proprioceptive deficits.

## INVESTIGATIONS

Haematological and biochemical test results were unremarkable. An MRI study of the head and cranial cervical spinal cord was performed under general anaesthesia. The MRI study (1.5 T Vantage Elan; Canon Medical Systems, the Netherlands) of the cranium and cranial cervical region was performed with a Flex Speeder medium-sized coil. Sequences included were dorsal inversion recovery, sagittal T2-weighted (T2W), sagittal 3D T1W, transverse T2W, transverse susceptibility weighted and transverse diffusion-weighted/apparent diffusion coefficient map sequences. After intravenous contrast administration (gadolinium, 0.15 mmol/kg), transverse T1W, sagittal 3D T1W and transverse fluid-attenuated inversion recovery (FLAIR) sequences were acquired. The images revealed multifocal T2W hyperintense, T1W hypointense

  

intradural lesions with intra-axial and intramedullary extension. The lesions were localised in the regions of the occipital and parietal lobes, midbrain, pons, cerebellum and cranial cervical spinal cord, most notably dorsally to the spinal cord at C1–C2 with marked spinal cord compression (Figure 1). Marked contrast enhancement was evident on postcontrast images. Dural tail signs were seen in most of the lesions.

There were no specific MRI findings suggestive of increased intracranial pressure or other contraindications to performing a cerebrospinal fluid (CSF) tap. Analysis of a CSF sample taken from the cisterna magna revealed a protein concentration of 2.01 g/L (reference range: <0.3 g/L), a total nucleated cell count of 276 cells/$\mu$l (reference range: <5/$\mu$l) and red blood cell count of 6 cells/$\mu$l (reference: 0/$\mu$l). Cytological examination showed a mixed pleocytosis. PCR for *Neospora caninum*, *Toxoplasma gondii*, distemper virus and *Bartonella* spp. and an ELISA for tick-borne encephalitis performed on CSF were all negative.

**LEARNING POINTS/TAKE HOME MESSAGES**

- Multifocal central nervous system signs can be caused by primary nervous system neoplasia.
- Papillary meningiomas in dogs can be multifocal.
- Papillary meningiomas in dogs are more rare than other histological subtypes, but can be very aggressive–similar to their human counterpart.
- Pseudo-rosette(-like) formations can be encountered in different types of central nervous system neoplasia, including papillary meningiomas.

## DIFFERENTIAL DIAGNOSIS

Differential categories considered after the MRI investigations were

- neoplastic (primary central nervous system [CNS] neoplasia with metastases [e.g., histiocytic sarcoma, lymphoma, leptomeningeal gliomatosis] or metastatic neoplasia of tumours outside of the CNS [e.g., meningeal carcinomatosis]);
- inflammatory (immune-mediated [e.g., granulomatous meningoencephalitis] or infectious [e.g., protozoal meningoencephalitis]).

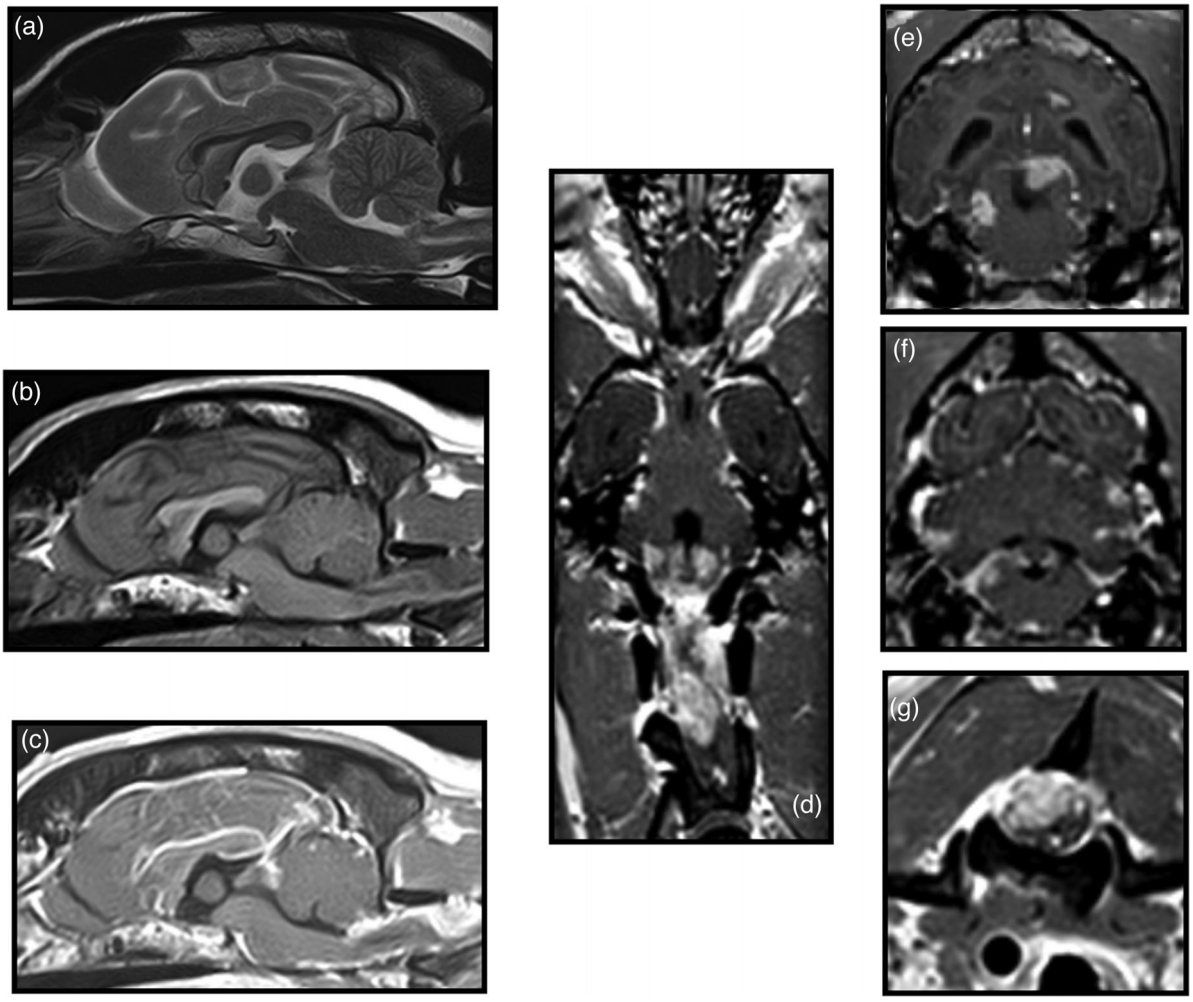


**FIGURE 1** Magnetic resonance images of the cranium and cranial cervical spinal cord. (a) Sagittal T2W FSE image. (b and c) Pre- and postcontrast sagittal 3D-SGE T1W images. (d) Reconstructed dorsal 3D-SGE T1W postcontrast image at the level of the fourth ventricle. (e–g) Reconstructed transverse 3D-SGE T1W postcontrast images at the level of the rostral colliculi, the fourth ventricle and C1–C2, respectively. Note the multifocal T2 hyperintense and contrast-enhancing lesions at the periphery of the neural parenchyma, with some locations showing signs of intra-axial/intramedullary invasion. Dural tail signs can be seen as well

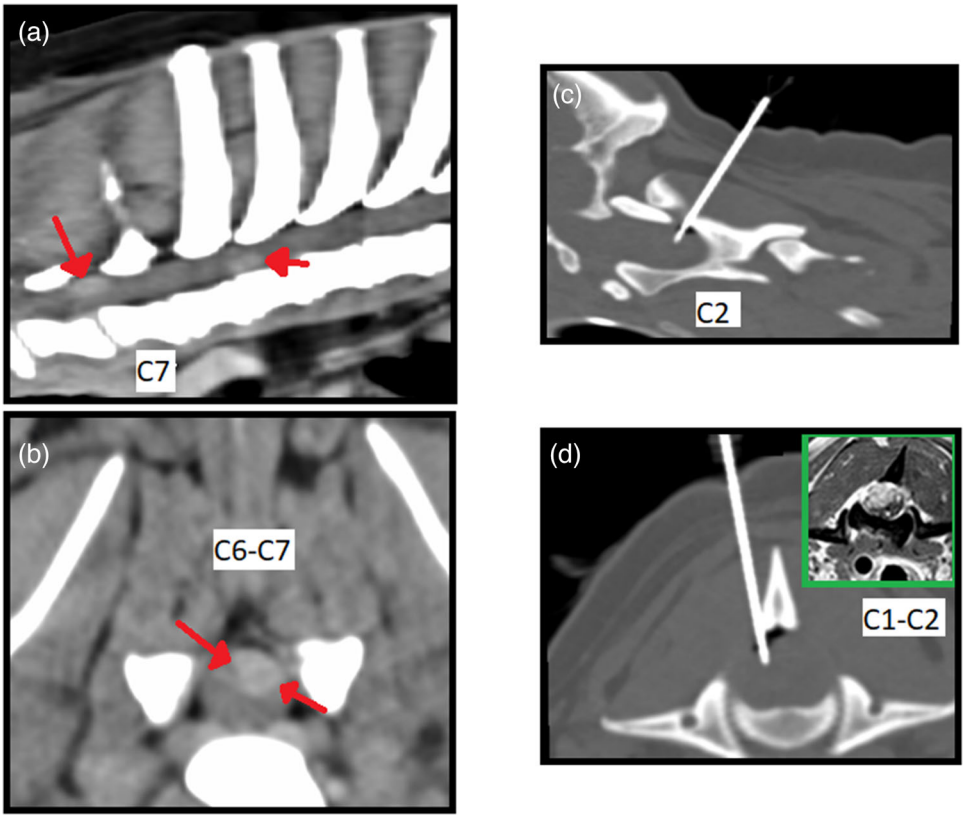


**FIGURE 2** Postcontrast computed tomography (CT) images of the cervicothoracic and cervical vertebral column and spinal cord. (a) Sagittal reconstruction (soft tissue algorithm, window width [WW] 400, window level [WL] 60) showing two enhancing intradural (possibly intramedullary) lesions (red arrows). (b) Transverse image (soft tissue algorithm, WW 400, WL 60 at the level of C6–C7 showing the broad-based contrast-enhancing lesion at that site. (c and d) Sagittal reconstruction (c) and transverse (d) (bone algorithm, WW 2500, WL 455) images showing the CT-guided fine-needle aspiration biopsy procedure being performed. These images confirm correct placement of the spinal needle within the mass (the inset shows the lesion in the corresponding MRI image, Figure 1g). A small amount of air is seen extradurally, dorsal to the spinal cord (iatrogenic)

Tests performed on CSF did not reveal neoplastic cells and did not show positive test results for infectious disease.

## TREATMENT

Treatment was started with 0.6 mg/kg prednisolone twice daily and 11 mg/kg clindamycine twice daily (discontinued after CSF test results).

## OUTCOME AND FOLLOW-UP

A favourable response was noticed after start of treatment, but recurrence and progression of signs were noticed 2 weeks later. Repeated neurological examination revealed increased severity of tetraparesis. The dosage of prednisolone was increased to 1.2 mg/kg twice daily, and a computed tomography (CT) scan of the thorax, abdomen and entire vertebral column was performed 3 days later, in conjunction with a CT-guided fine-needle aspiration biopsy (FNAB) of the C1–C2 lesion (Figure 2). Postcontrast CT scan of the cervicothoracolumbar spinal cord showed additional multifocal lesions. Pre- and postcontrast CT studies did not show signs of intrathoracic or abdominal neoplasia. The cytological examination of the FNAB sample showed round and spindle-shaped neoplastic cells with anisokaryosis and central nucleoli (Figure 3). The cells were suspected to be of mesenchymal lineage. Recovery from anaesthesia was without complications and the dog's clinical status was unchanged afterwards. Three days later, the owners noticed further progression of clinical signs (progressive tetraparesis, difficulty eating/swallowing and breathing) and elected euthanasia. Postmortem examination of the brainstem and spinal cord revealed intradural mass lesions (Figure 4). Microscopical examination showed multifocal, strongly intra-axial and intramedullary infiltrative growth of neoplastic cells with areas of pseudo-rosette formation by cylindrical neoplastic cells in a papillary pattern, with moderately large, oval nuclei, and frequent mitotic figures in addition to areas of spindle-shaped neoplastic cells with meningothelial whorls consistent with a transitional pattern (Figure 5). Immunohistochemistry (IHC) for vimentin showed strong cytoplasmic staining. These findings were consistent with PM with multifocal (suspected cranial and caudal) leptomeningeal spread.

## DISCUSSION

PM is considered a rare tumour in humans.[6,7] In a recent retrospective canine study by Mandara et al., 19 out of 121 cases (15.7%) of histopathologically confirmed meningiomas were classified as PM with a male/female ratio of 1.7.[8] A total of 16 cases were included for analysis in that study. In two cases, spinal cord tumours were reported. No cases with multifocal leptomeningeal spread were reported. Eight dogs were treated surgically, of which seven experienced recurrence of tumour growth, with a median survival time of 8.5 months (range 4–

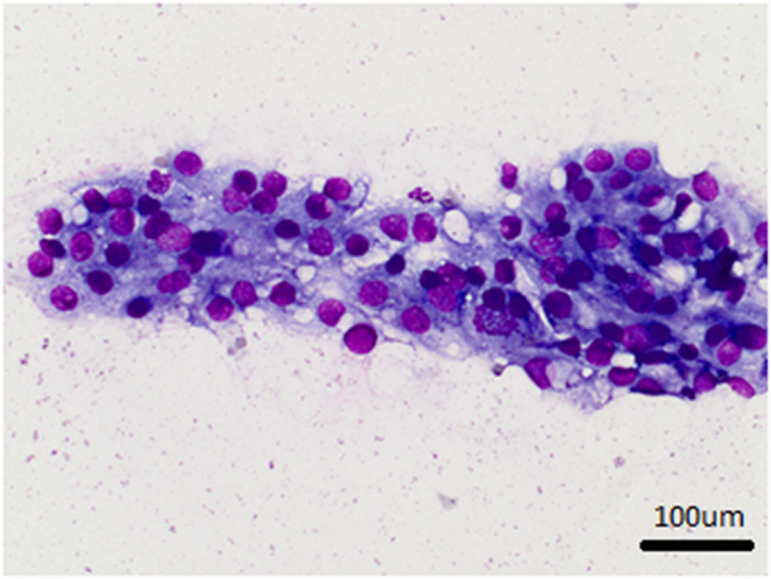


**FIGURE 3** Stained (Romanowsky stain variant) cytological preparation of the fine-needle aspiration biopsy sample. The sample contains round and spindle-shaped neoplastic cells with anisokaryosis and central nucleoli

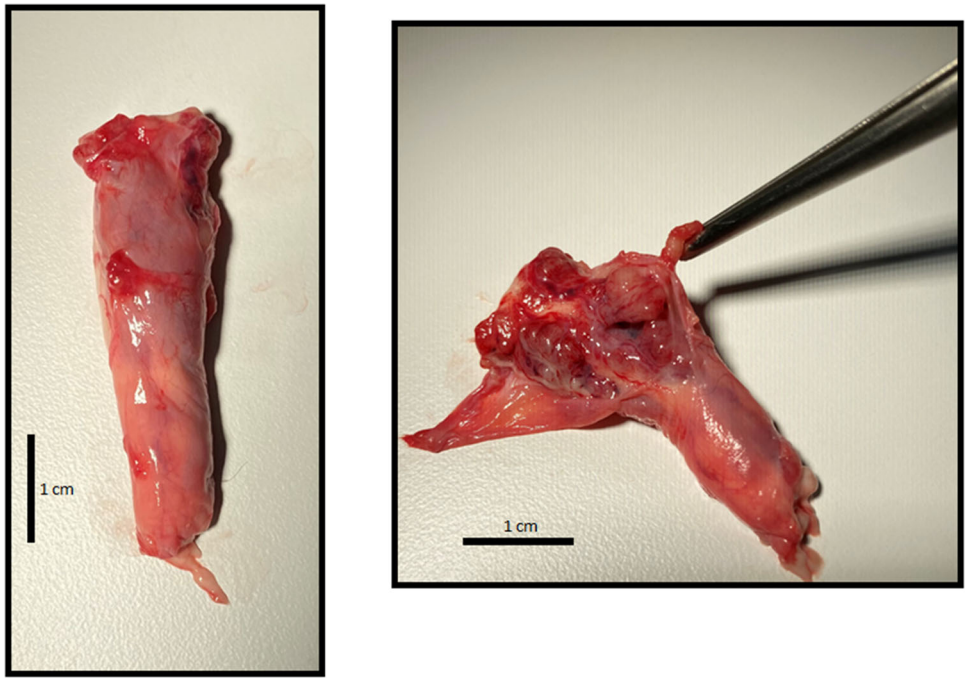


**FIGURE 4** Fresh postmortem-acquired cervicomedullary junction. The left image shows the tissue with the dura mater intact. The right image shows the mass lesions (reddish) after cutting and reflection of the dura mater. The forceps grasp the C1 spinal nerve

24 months) and eight dogs were treated conservatively with a median survival time of 7 days (range 1–90 days). Median post-surgery survival time for meningothelial, fibroblastic and transitional meningiomas from patients of the same database used in that study was 24–27 months. Pseudo-rosette-like formation was reported in that study when papillary figures were transversely sectioned. As in our case, the papillary pattern could be seen in addition to other histological patterns, such as transitional or fibrous patterns. In the study by Mandara et al., the diagnosis of PM was substantiated using IHC for E-cadherin, N-cadherin and doublecortin.[8] Vimentin positivity is reported in 100% of canine meningiomas.[9] IHC results, in conjunction with histological characteristics in the haematoxylin and eosin stain, and localisation of the masses were deemed sufficient for diagnosing a PM, and additional IHC was therefore not performed in our case.

In a recent review of histological grading systems in veterinary medicine, the grading system of meningiomas was discussed among a large number of other types of neoplasia.[4] That grading system is based on the human classification system of meningiomas in which the histological subtype of PM is classified as grade III.[2–5] Veterinary grading systems are currently under discussion and will likely be subject to revision based on developments in human as well as veterinary medicine.[4,5,10] The presence of papillary features in human meningiomas justifies a grade III classification. Molecular characterisation may allow for more accurate classification of meningiomas.[5]

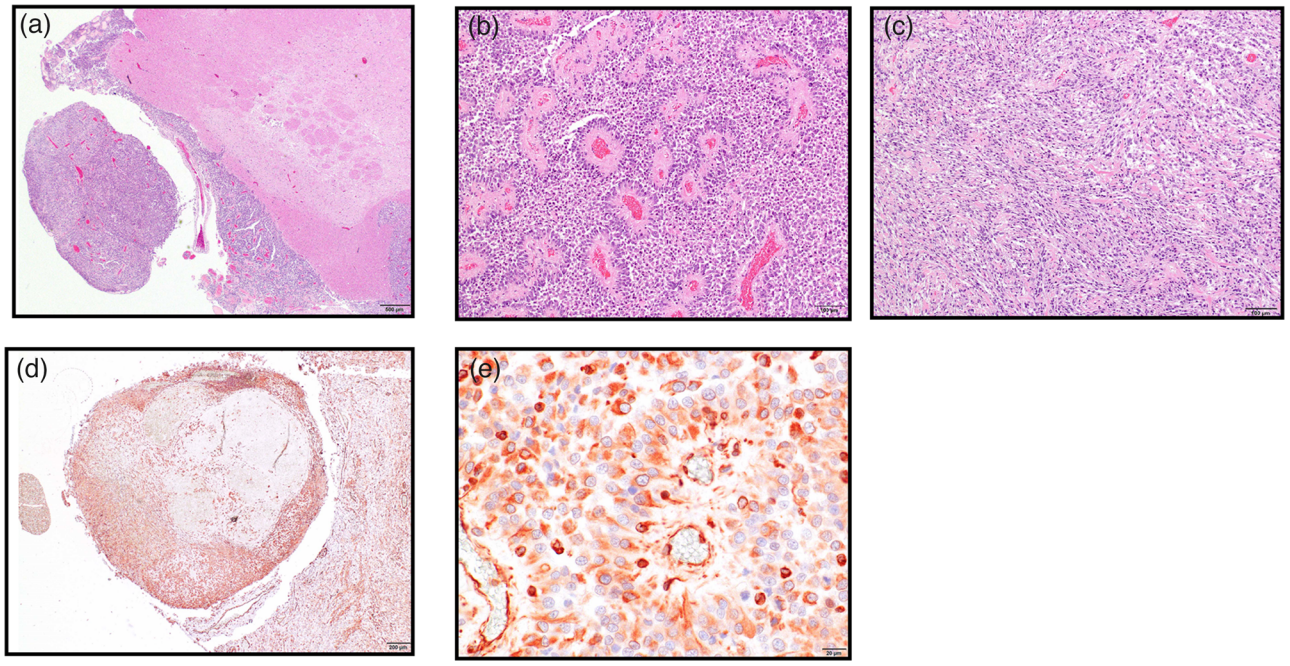


**FIGURE 5** Histological microphotographs of the lesions. (a) A nerve root (left), meninges and parenchyma are invaded by neoplastic cells. Haematoxylin–eosin. Scale bar: 500 $\mu$m. (b) A region showing pseudo-rosette formation and a papillary pattern of tumour tissue. Haematoxylin–eosin. Scale bar: 100 $\mu$m. (c) A region showing meningothelial whorls and a transitional pattern of tumour tissue. Haematoxylin–eosin. Scale bar: 100 $\mu$m. (d) Neoplastic cells in a nerve root expressing strong positivity for vimentin. Vimentin immunohistochemistry. Scale bar: 200 $\mu$m. (e) Neoplastic cells in a papillary pattern region of the tumour expressing strong positivity for vimentin. Vimentin immunohistochemistry. Scale bar: 20 $\mu$m

Pseudo-rosette and rosette formation is a typical finding of ependymomas.[11] Importantly, PM, among other CNS tumour types, has been reported as a possible mimic. This is vital for neuropathologists to realise, as they may form a pitfall in diagnosing these tumours accurately. Although typical for meningiomas, the MRI finding of a 'dural tail sign' is not pathognomonic for this tumour, as other tumours may show this sign as well.[12]

Multifocal spinal PM has been reported in a dog before, although multifocal intracranial and spinal PM, to the authors' knowledge, has not.[13] In that reported case, cytological examination of intraoperatively acquired samples showed mesenchymal neoplasia. The case reported here describes the MRI findings of PM with multifocal leptomeningeal spread for the first time.

Leptomeningeal metastasis, leptomeningeal spread or 'drop-metastasis' is defined as the appearance of tumour cells in the leptomeninges or CSF distant from the site of a primary tumour.[13] Leptomeningeal spread is a clinically relevant and possibly devastating finding, with implications for treatment options and prognosis in humans.[6,7,14] Leptomeningeal spread of choroid plexus carcinomas and glial tumours has been described in dogs.[12,15,16] Usually, metastasis or spread occurs in the direction of CSF flow, which is mostly caudal. However, in this case, we suspected that the primary mass lesion was located at C1–C2 as described, as this was the largest neoplastic mass encountered. Cranial and caudal leptomeningeal spread is reported in human medicine.[10] However, size alone is not a confirmation of a lesion being the primary tumour site, so this remains speculative in our case.

The neurolocalisation in this case was multifocal intracranial, possibly including the cervical spinal cord, at least with involvement of central vestibular systems. The actual identified lesions were indeed multifocal, involving the telencephalon, mesencephalon, metencephalon (pons and cerebellum), cranial cervical spinal cord, cervicothoracic and lumbar spinal cord. These locations can explain the clinical findings. However, not all identified sites of the lesions were evident clinically. Several studies report on the reliability of the clinical neurological examination with regard to localisation (neurolocalisation).[17-22] From those studies, it is clear that the neurolocalisation is not always entirely accurate and that lesions may be clinically 'silent'.

Regarding the FNAB performed in this case, this procedure was planned after discussion with the owners on how to get a sample of the lesion without having to resort to surgery (according to the owners' wishes). If the FNAB would be able to differentiate between neoplasia and an inflammatory lesion, this would provide important information for prognostication and treatment options or a discussion to euthanise the dog. For instance, if a diagnosis of lymphoma would have resulted from the FNAB, this would have led to considerations of chemotherapy. Although uncommonly performed, the dorsal localisation of the lesion at C1–C2 and its relatively large size were considered positive factors for an attempt at acquiring an FNAB. The risks of performing an FNAB at this location (e.g., spinal cord injury at this site by either direct puncture, laceration or haemorrhage due to needle placement) were discussed as well. After careful consideration, the owners decided to have the procedure performed.

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## CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

## ETHICS STATEMENT

Ethical approval was not applicable to this case report.

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