Clinical, imaging and histopathological characteristics of a malignant intracranial meningioma with pulmonary metastasis in a dog

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Abstract
A 13-year-old Spanish Breton was presented for a hyperacute onset of dull mentation followed by a generalised tonic-clonic seizure and recumbency. An intracranial magnetic resonance imaging study identified a well-demarcated intraventricular mass, and cerebrospinal fluid analysis revealed moderate neutrophilic pleocytosis and proteinorachia. A tentative diagnosis of meningioma was made and medical treatment was started. After a short initial improvement, the patient died 3 weeks later. Histopathology confirmed the presence of a malignant meningioma (World Health Organization grade III) and pulmonary metastasis. This is, to our knowledge, the first reported case of a canine intracranial meningioma with pulmonary metastasis showing magnetic resonance imaging and immunohistochemical characterisation of the tumour.

BACKGROUND
Meningiomas are common intracranial neoplasms derived from meningotheelial cells, which have been well described in the veterinary literature. They are usually slow growing, benign tumours that account for 45% of all primary intracranial tumours in dogs. Based on the human World Health Organization (WHO) classification, most canine meningiomas are histologically classified as benign (56%) or grade I. Grade II or atypical meningiomas are 43% of all of them, and grade III or anaplastic variants are the least common, accounting for 1%. Distant metastasis of intracranial meningiomas is extremely rare, with less than 1% reported in humans, and just one study in dogs describing three cases.

CASE PRESENTATION
A 13-year-old, male, neutered Spanish Breton was presented to the veterinary hospital for a hyperacute onset of dull mentation followed by a generalised tonic-clonic seizure. The owner also described a dramatic change in the patient’s mental status the same morning of the presentation. The dog was very quiet and less responsive than normal early in the morning, and progressed to show incoordination and hypersalivation during the next few hours. At night, the dog’s mentation was severely depressed and a generalised tonic-clonic seizure developed. By then, the owner decided to take dog to the veterinary hospital. Before this event, no abnormalities had been observed. Abnormal findings on physical examination included tachypnoea, tachycardia and hyperthermia (39.7°C). Neurological examination showed dull mentation, ambulatory tetraparesis with generalised proprioceptive ataxia and absent proprioceptive positioning in all four limbs. Menace response was inconsistent in the left eye, and nasal mucosa sensation was decreased on the left side. Neuroanatomical localisation was right prosencephalon. Differential
diagnoses included vascular accident, intoxication, neoplasia, inflammatory/infectious or, less likely, metabolic disease.

INVESTIGATIONS

Blood tests, urinalysis and abdominal ultrasound revealed no abnormalities, but thoracic radiographs showed a multiple nodular pattern scattered throughout both lungs (Figure 1a,b). MRI of the brain was performed using a 0.4 Tesla permanent magnet unit (Hitachi Aperto Lucent Hitachi Medical Systems, Madrid, Spain). Sequences performed included T2-weighted images (WI) in transverse, sagittal and dorsal planes; pre- and postcontrast T1-WI in transverse and sagittal planes; T2-weighted fluid attenuated inversion recovery images (T2-FLAIR), and T2*-WI in transverse plane. Gadolinium (Dotarem 0.5 mmol/ml, Dotarem-Guerbet Laboratories, Madrid, Spain) was the contrast agent used at a dose of 0.1 mmol/kg intravenously (IV).

Imaging identified a single, well-defined intraventricular mass located in the midline and dorsal to the thalamus. The mass was round to oval in shape, and measured 2.13 cm craniocaudally, 1.40 cm dorsoventrally and 2.40 cm transversely. It was heterogeneously hyperintense on T2-WI and T2-FLAIR, and iso- to hypointense on T1-WI compared to the normal gray matter. Contrast enhancement was marked and homogeneous (Figure 2a–f). Mass effect was identified causing collapse of the lateral ventricles in their central portion, and thalamic compression with caudoventral displacement of cerebral parenchyma. The cerebellum was flattened in its rostral aspect, and it was mildly compressed by the caudal colliculus, which was displaced caudally. Moderate generalised effacement of the cerebral sulci was also observed.

Cerebrospinal fluid (CSF) was collected from the cerebellomedullary cistern and analysis revealed a moderate neutrophilic pleocytosis (60 WBC/µl; reference range ≤5 WBC/µl), and proteinorrachia (864 mg/dl; reference range <30 mg/dl). No microorganisms were identified on cytological examination.

LEARNING POINTS/TAKE-HOME MESSAGES

- Malignant meningiomas are very rare in both dogs and humans.
- Distant metastases of intracranial meningiomas are even more unusual in both dogs and humans.
- Primary and metastatic meningiomas are expected to immunostain positively to S100 protein and vimentin, and they are expected to be negative to glial fibrillary acidic protein, epithelial membrane antigen and cytokeratins.
- To the authors’ knowledge, this is the first report describing a canine intraventricular malignant meningioma with pulmonary metastasis and its magnetic resonance imaging and immunohistochemical features.
- Although rare, malignant meningiomas should be considered, and the presence of metastasis should be ruled out in patients with meningiomas.

DIFFERENTIAL DIAGNOSIS

Choroid plexus tumour, ependymal tumour or meningioma are the main differential diagnoses for ventricular tumours. Intraventricular neurocytoma and lymphoma have also been described.

TREATMENT

The patient was hospitalised and palliative medical treatment with anti-inflammatory doses of prednisone (0.5 mg/kg IV every 24 hours), phenobarbital (3 mg/kg IV every 12 hours) and diazepam in case of seizures (1 mg/kg IV) was started. Radiation therapy was rejected by the owner.
**FIGURE 2** Magnetic resonance images (MRI) of the intraventricular meningioma. Transverse T2-weighted images (WI) (a), T1-WI (b) and T1-WI postcontrast (c) images; and sagittal T2-WI (d), T1-WI (e) and T1-WI postcontrast (f) sequences. A well-defined mass, round to oval shaped, is present within the lateral ventricles. It is heterogeneous and hyperintense on T2-WI (a and d), iso- to hypointense on T1-WI images (b and e), and strongly contrast enhancing (c and f). It measures 2.13 × 1.4 × 2.4 cm (craniocaudally × dorsoventrally × transversely) and causes a moderate mass effect displacing and compressing adjacent structures (0.4 T MRI system).

**OUTCOME AND FOLLOW-UP**

The dog’s neurologic condition improved progressively, and no further seizures were observed for the rest of the days of hospitalisation. The patient was discharged 4 days after admission with mild generalised proprioceptive ataxia, but the rest of the neurological examination was unremarkable.

A week later, the neurological examination was normal on recheck appointment and the owner reported a positive progress. The third week after discharge, there was an acute worsening of clinical signs. The owner described a sudden onset of dull mentation, constant panting and recumbency, and sudden death 1 hour later on his way to the hospital.

A postmortem examination, authorised by the owner, was performed. On gross examination of the brain, a well-circumscribed and firm intraventricular mass was identified (Figure 3). Several firm nodules were also identified in the lungs, spreading over all lobules (Figure 4).

Microscopic examination of the brain mass evidenced a non-encapsulated but well-defined neoplastic cell proliferation of fusiform cells with a solid growth pattern (Figure 5a). Abundant and wide necrotic areas, with a large number of active macrophages and neutrophils and several blood vessels, were present (Figure 5b). The cells were medium to large, with a big round or irregular nucleus, lax chromatin and sometimes apparent nucleoli (Figure 5c). The cytoplasm was scarce, but eosinophilic when evident. Anisocytosis, anisokaryosis and numerous mitoses were found. The neoplastic population followed a perivascular and papillary pattern. The perilesional brain parenchyma showed microspongiosis, diffuse and reactive gliosis and perivascular cuffs of inflammatory and neoplastic cells.

The pulmonary nodules consisted of neoplastic proliferations of similar fusiform cells, with more pleocytosis than those in the brain. The nodules were non-encapsulated.
FIGURE 4  Macroscopic view of the fresh lungs. Several firm nodules, from 2 to 4 cm diameter (arrows), are seen throughout the parenchyma, spreading among all lobules but well delimited, and compressed the lung parenchyma (Figure 5e). Marked anisokaryosis with large and ovoid or lobed nucleus and elongated eosinophilic cytoplasm were present (Figure 5f,g). Mitoses were frequent. The growth pattern included solid areas of neoplastic cells organised in dense bundles, mixed with areas in which neoplastic cells were surrounding an eosinophilic material made of necrotic cellular debris, with the presence of a purulent inflammatory infiltrate.

A Masson’s trichrome stain of the brain sections evidenced the presence of scarce collagen fibres mainly located in the perivascular spaces. In the lung mass, large amounts of collagen fibres were found between the neoplastic cell population.

Immunohistochemistry was also used to characterise the neoplastic cell population. On brain sections S100 protein immune-stained positively up to 60% of cells (Figure 5d), and up to 80% of cells stained positively in the pulmonary mass (Figure 5h). Small numbers of neoplastic cells were positive to vimentin (VIM) in the encephalic mass, but 40%–60% of neoplastic cells were positive to the same marker in the pulmonary mass. No positivity was observed (brain or lung) to glial fibrillary acidic protein (GFAP), epithelial membrane antigen (EMA) or cytokeratins (CK).

The findings were consistent with a malignant brain meningioma (WHO grade III) with pulmonary metastasis.

DISCUSSION

This report describes the clinical, imaging and histopathological characteristics of a malignant meningioma with pulmonary metastasis in a dog.
Malignant meningiomas are uncommon in dogs. Of 112 dogs with intracranial meningiomas in a study published by Sturges et al., just one of them was classified as malignant. A similar review indicating that malignant meningiomas represent 1%–3% of all meningiomas. Intracranial meningiomas with metastatic spreading to extra-CNS organs are even less common. In dogs, just a prior study reported the clinicopathological features of intracranial meningiomas with pulmonary metastasis in three dogs and the CT images in two of them, but no MRI study or immunohistochemical characterisation was performed in any of them.

The MRI characteristics of the mass described herein were identical to those reported for intracranial meningiomas. The mass was large and occupied more than 25% of the cranial volume. However, the MRI features of meningiomas cannot predict the pathological grade or the potential growth of the neoplasm. In human medicine, a large tumour volume is the most reliable predictor for high-grade meningioma. In fact, Magill et al. found that tumour sizes greater than 3.2 cm increased the likelihood of being WHO grade II instead of WHO grade I meningiomas. In our case, the tumour diameter was 2.40 cm, which was a significant size for a dog's brain.

Neutrophilic pleocytosis in the CSF analysis has been frequently associated with intracranial meningiomas. However, Dickinson et al. published a retrospective study of 56 dogs with intracranial meningioma and identified neutrophilic pleocytosis in only 19% of them. In addition, it was less likely in animals with meningiomas located within the mid or rostral portions of the cranial fossa. In the case described here, the meningioma was located within the lateral ventricles, and a moderate neutrophilic pleocytosis was identified in the CSF analysis.

Clinical signs associated with meningiomas are related to localisation, size and the presence of secondary changes (oedema, necrosis and inflammation). In the clinical case described here, the response to corticosteroids was most likely due to a reduction of secondary vasogenic oedema. The main goal of phenobarbital was to reduce the frequency and the severity of tumour-associated seizures.

Histopathology confirmed that the tumour was a malignant meningioma with pulmonary metastasis, and that the neoplastic cells in the lungs had even more malignant characteristics than those in the brain. These findings were similar to those reported in one of the three cases described by Schumman et al. The immunohistochemical reaction to S100 protein was similar to the one described in human high-grade meningiomas, and the VIM immune-stained positive results also confirmed the leptomeningeal origin of these cells.

To the best of our knowledge, this is the first description of the imaging and immunohistochemical characteristics of a primary malignant meningioma and its pulmonary metastases in a dog.

**IMAGE QUIZ**

Figure 1 Thoracic radiographs. Right lateral (a) and ventrodorsal view (b). In both hemithoraxes, multiple nodular structures of soft tissue opacity, small size, rounded shape and moderately defined edges are observed.

**MULTIPLE CHOICE QUESTION**

What is the likely diagnosis?

**POSSIBLE ANSWERS TO MULTIPLE CHOICE QUESTION**

a) Fungal granulomas
b) Parasitic granuloma
c) Pulmonary abscesses
d) Primary pulmonary neoplasia (adenocarcinoma, carcinoma, squamous cell carcinoma or anaplastic carcinoma)
e) Metastatic pulmonary neoplasia (meningioma)

**CORRECT ANSWER**

e) Metastatic pulmonary neoplasia (meningioma).

A primary malignant intracranial meningioma with pulmonary metastases was diagnosed in this dog. It has been described (in a very few cases) as 0.5–4 cm diameter, firm, round-shaped nodules scattered throughout both lungs. It is an unusual presentation, but pulmonary metastasis should be ruled out in patients with meningiomas.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**ETHICS STATEMENT**

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a case report article with no original research data. The owner gave informed written consent for all the investigations.

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