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Cerebral meningioma associated with extensive calvarium osteolysis and presumed intratumoral carcinoma metastasis in a cat

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Abstract

Case summary A 10-year-old male neutered domestic shorthair cat presented with a 3-month history of weight loss, dysorexia and lethargy. Neurological examination revealed decreased mentation, absent menace response bilaterally and proprioceptive deficits affecting all four limbs; these findings were consistent with a forebrain disorder. Brain CT revealed an extensive asymmetric permeative osteolysis destroying two-thirds of the circumference of the calvarium and involving the right frontal, parietal, temporal and occipital bones, as well as the left parietal bone. This extensive bone lysis was associated with a large 'plaque-like' extra-axial subdural/pachymeningeal lesion extending within the soft tissues surrounding the calvarium. The cat was humanely euthanased. Post-mortem MRI was performed, which revealed a T2-weighted (T2W) hypointense subdural lesion and a T2W hyperintense circumferential extracranial lesion lining the right calvarium and left parietal bone. Histopathological analysis on a post-mortem sample of the lesion revealed a fibroblastic subtype of meningioma. Epithelial neoplastic cells were observed scattered through the meningioma, calvarium and surrounding muscular tissues, corresponding with presumed metastatic carcinoma.

Relevance and novel information To our knowledge, this is the first report of an intracranial meningioma associated with such an extensive and diffuse calvarial osteolysis in veterinary medicine. This is also the first description of presumed metastatic inclusions (adenocarcinoma in this case) inside an intracranial feline meningioma, which is a rare phenomenon known as tumour-to-tumour metastasis in human medicine.

Keywords: Meningioma; bone lysis; tumour-to-tumour metastasis; adenocarcinomatous metastasis; calvarium; calvarial destruction

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Case description

A 10-year-old male neutered domestic shorthair cat was presented with a 3-month history of weight loss, dysorexia and lethargy. Haematology and biochemistry were normal. The cat was first treated with meloxicam (0.05 mg/kg PO q24h [Meloxidyl; CEVA]) for 7 days without success and started to develop neurological signs.

The cat was then referred to our hospital. Physical examination revealed a lethargic animal without other significant signs. Neurological examination revealed decreased mentation and moderate proprioceptive deficits affecting all four limbs with normal spinal reflexes. Its gait was difficult to assess because the cat was unwilling to move, but it seemed normal. Menace response was decreased bilaterally, with normal pupillary light reflexes.

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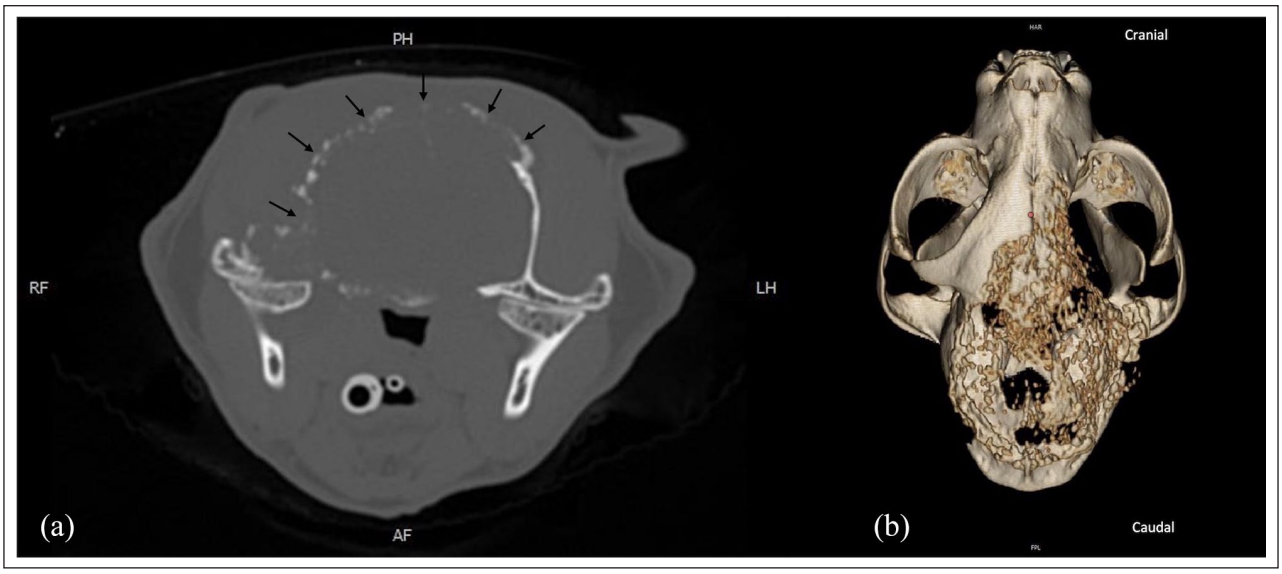

Figure 1 Bone reconstruction of a transverse CT scan (a) and three-dimensional reconstruction (b) images of the cat's skull showing an extensive asymmetric permeative osteolysis affecting two-thirds of its circumference (arrows)

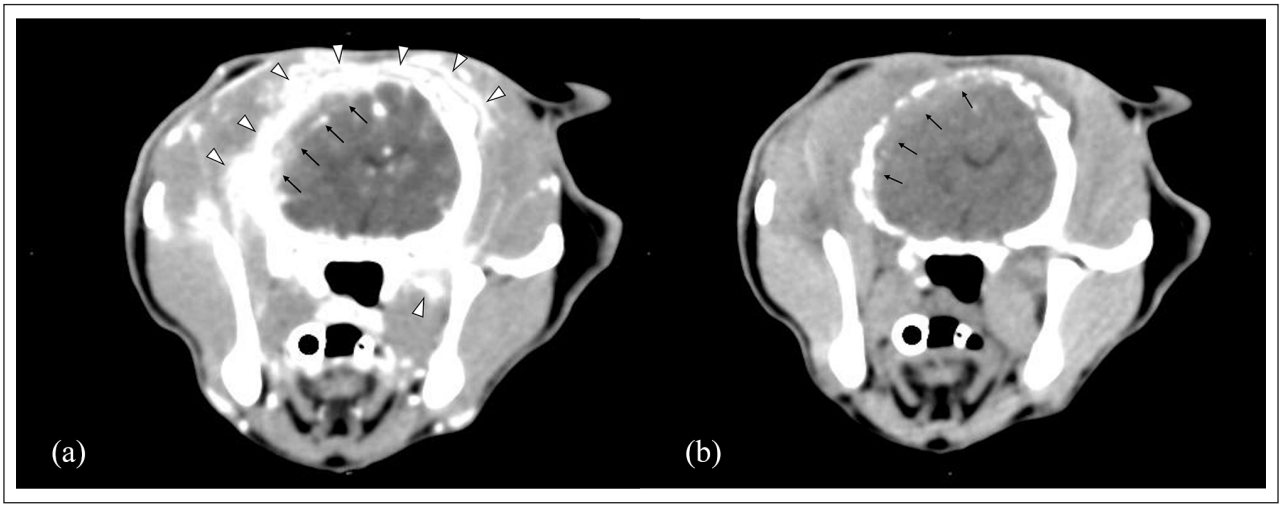

Figure 2 (a) Transverse precontrast CT image of the cat's brain, at the level of the caudate nuclei showing a large 'plaque-like' extra-axial subdural/pachymeningeal, mildly hyperattenuating lesion (arrows). (b) Transverse postcontrast CT image of the lesion described in (a), showing moderate heterogeneous contrast enhancement (arrows). The lesion is shown to extend into tissues surrounding the calvarium, inducing an irregularly contrast-enhancing periosteal reaction along the right temporal, parietal, left parietal and ventral basisphenoid bone (arrowheads)

These findings were consistent with a forebrain lesion. Preanaesthetic abdominal ultrasonography and thoracic radiographs were unremarkable. A pre- and post-contrast (iohexol 350 mgI/ml 2 ml/kg IV [Omnipaque, GE Healthcare]) CT (Brilliance; Philips) study of the brain was performed and reviewed by a board-certified radiologist. After induction with propofol (4 mg/kg IV) and diazepam (0.5 mg/kg IV), anaesthesia was maintained with isoflurane and oxygen. An extensive asymmetric permeative osteolysis affecting two-thirds of the circumference of the calvarium was observed, involving the right frontal, parietal, temporal (zygomatic arch, retroarticular process and mandibular fossa) and occipital bones, as well as the left parietal bone (Figure 1). An irregular periosteal reaction was observed along these bones; it was more pronounced on the occipital bone. Bone lysis of the presphenoid and basisphenoid bones was also present with irregular spiculated periosteal reaction on the ventral aspect of the basisphenoid bone. This extensive bone lesion was associated with a large 'plaque-like' contrast-enhancing extra-axial subdural/pachymeningeal lesion, extending within the tissues surrounding the calvarium (Figure 2a,b). A severe mass effect was observed, resulting in a subtentorial herniation

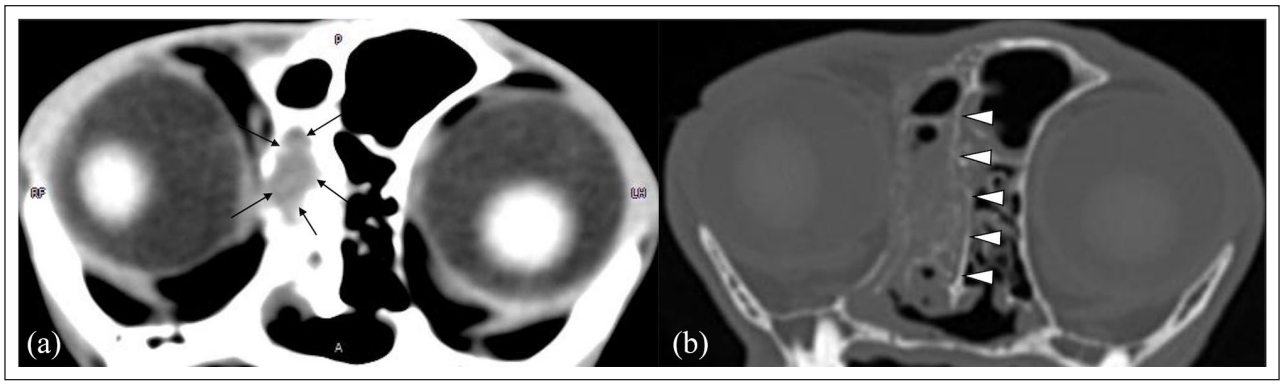

Figure 3 (a) Transverse CT image of the contrast-enhancing soft tissue-attenuating material partially filling the right nasal cavity (arrows). On the bone reconstruction image (b), slight deviation of the nasal septum to the left side (arrowheads) and secondary nasal turbinate rarefaction are observed

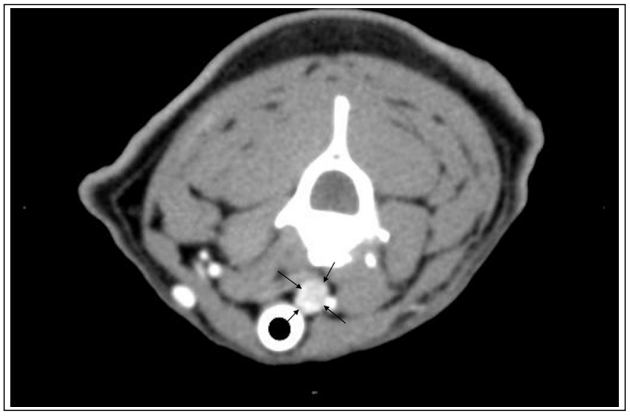

Figure 4 Transverse CT image of the contrast-enhancing nodule affecting the left thyroid gland (arrows)

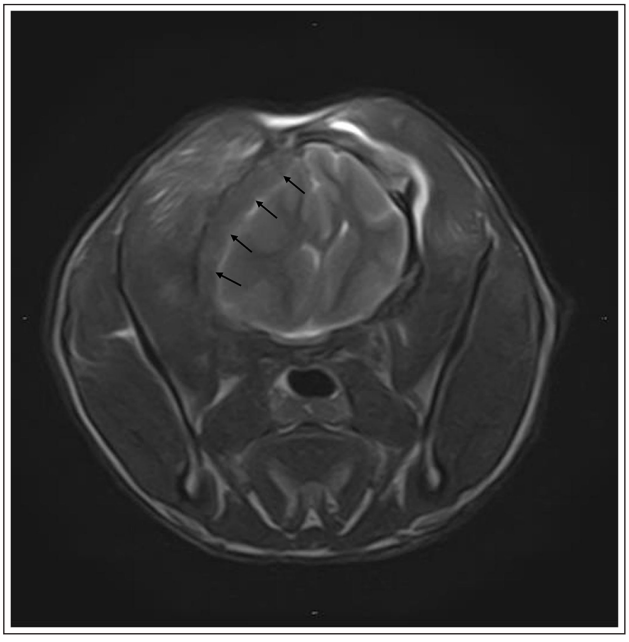

Figure 5 Transverse T2-weighted image of the cat's brain at the level of the caudate nuclei, showing the same extra-axial subdural lesion described in Figure 2(a), which appears hypointense (arrows). Severe mass effect is observed, resulting in a marked compression and displacement of the adjacent brain parenchyma toward the left and a deviation of the falx cerebri to the left side

and a cerebellar herniation through the foramen magnum. The left frontal sinus was enlarged and the right sinus was missing, most likely due to congenital anomaly. The nasal cavity was partially filled with contrast-enhancing soft tissue-attenuating material associated with nasal turbinates rarefaction. The nasal septum was slightly deviated to the left side (Figure 3). Soft tissue material was observed within the nasopharyngeal meatus, rostral nasopharynx and right presphenoid sinus. A contrast-enhancing nodule affecting the left thyroid gland was also noted (Figure 4).

Based on these findings (especially the calvarial osteolysis), an osseous or intracranial tumour was primarily suspected. CT was extended to the thoracic and abdominal cavities, searching for potential metastasis, but it did not reveal any further lesions. Given the extensive nature of the brain lesion and the poor prognosis, the cat was euthanased at the owner's request following the CT examination.

A post-mortem MRI of the brain was performed using a 1.5 T magnet (Vantage Elan; Canon-Toshiba) and was reviewed by a board-certified neurologist and a board-certified radiologist. T2-weighted (T2W) images were acquired in transverse, sagittal and dorsal planes. Three-dimensional T1-weighted and fluid attenuation inversion recovery (FLAIR) images were acquired in the transverse plane. The previously described right-sided extra-axial subdural lesion appeared homogeneously hypointense on T2W and FLAIR images. A severe mass effect was observed again, resulting in a marked compression and displacement of the adjacent brain parenchyma toward the left, and a deviation of the falx cerebri to the left side (Figure 5). On the sagittal images,

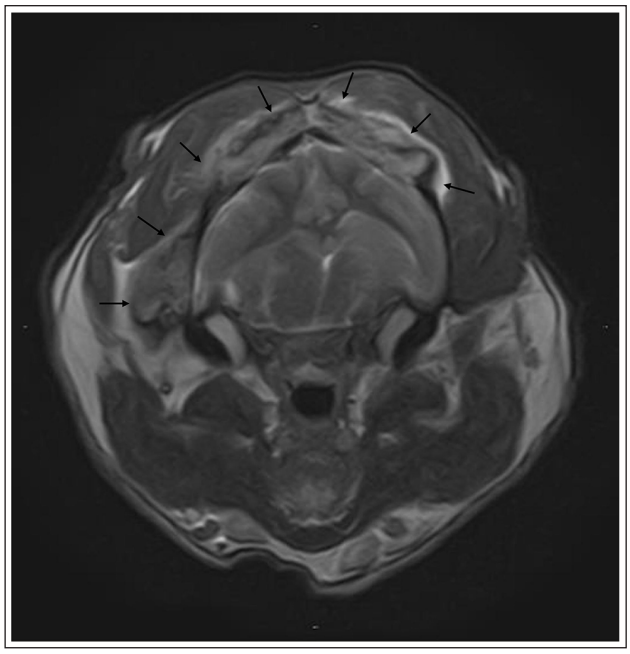

Figure 6 Transverse T2-weighted image of the cat's brain at the level of the thalamus, showing a heterogeneously hyperintense extracranial lesion surrounding the calvarium (arrows)

a diffuse, ill-defined, intramedullary T2W hyperintensity affecting the first cervical spinal cord segments was also noted, presumably resulting from the previously described cerebellar herniation through the foramen magnum. The extracranial lesion surrounding the calvarium appeared heterogeneously hyperintense on T2W and FLAIR images (Figure 6).

The owners declined a full necropsy but gave their consent for a focal sampling of the lesion. After a right dorsolateral approach of the calvarium, a right temporal bone incision was easily performed with a simple scalpel, given the pronounced bone lysis. A 2×2 cm sample (calvarium with adjacent soft tissues) was collected and examined by a board-certified pathologist. Macroscopically, a thinned crumbling and almost transparent calvarial bone was observed. In addition, the inner part of the sampled portion of the calvarium was lined with a thick greyish material with a firm consistency.

Histopathological examination revealed a moderately cellular neoplasm composed of spindle-shaped cells with elongated nuclei. The neoplastic cells were organised in bundles, streams and a few whorls, supported by a variably dense fibrovascular stroma (Figure 7). These findings were consistent with a fibroblastic subtype of meningioma. The mitotic count on a contiguous 2.37 mm^2 area was 08. The cytological atypia were limited. A few epithelial neoplastic cells were observed, forming tubules, with a cuboidal-to-polygonal shape, compatible with metastatic adeno- carcinoma. These

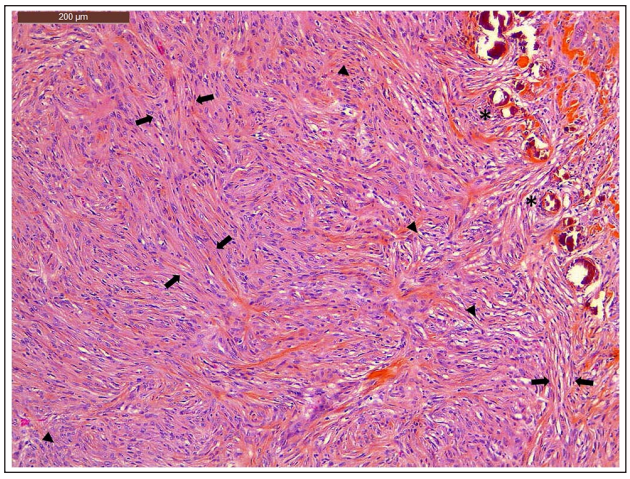

Figure 7 Histopathology of the extra-axial subdural lesion, revealing neoplastic cells organised in bundles (arrowheads), streams (arrows) and a few whorls (asterisks) with a variably dense fibrovascular stroma, compatible with a fibroblastic subtype meningioma (haematoxylin, eosin and saffron × 100)

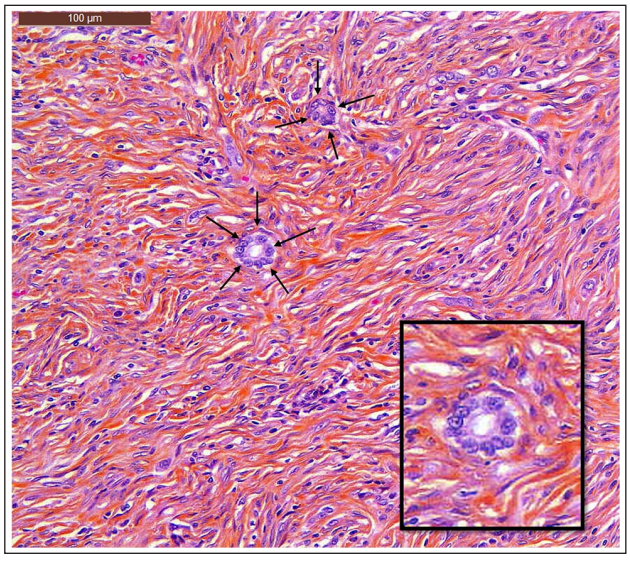

Figure 8 Presumed metastatic adenocarcinomatous inclusions (black arrows) inside the meningioma (haematoxylin, eosin and saffron × 200)

cells were scattered through the meningioma, and also the calvarium and surrounding muscular tissues (Figure 8). Cell atypia were mild, and no mitotic figure was recorded.

The final diagnosis was a cerebral meningioma associated with extensive lysis of the calvarium and presumed intratumoral adenocarcinomatous metastatic inclusions.

Discussion

Meningiomas are the most common primary tumours of the central nervous system (CNS) in cats, presumably

arising from the arachnoid granulations. In cats, meningiomas are often localised in the cerebral convexities and usually form well-demarcated extra-axial masses.[1,2]

Another common characteristic of feline meningiomas is hyperostosis, which can occur in up to 50% of cases.[3–5] The precise mechanism by which hyperostotic changes occur remains unclear. In human medicine, hyperostosis is thought to be the result of bone infiltration by tumour cells. This causes secondary changes in osteoblasts and osteoclasts activity, leading to increased bone deposition.[6] Some authors have also suggested a direct stimulation of bone deposition through a humoral network, involving alkaline phosphatase or insulin-like growth factor 1.[7,8] In contrast, the tumour reported here did not produce any hyperostotic changes, but was associated with the destruction of two-thirds of the calvarium, resulting in an extensive osteolysis of various bones. Meningioma-induced calvarium osteolysis has been previously described, to a lesser extent, in five cats and two dogs.[9–13] In those cases, erosion of the calvarial bone was restricted to a rather focal area adjacent to the meningioma, resulting in a limited extracranial expansion of the tumour through the bony defect. In our patient, an extracalvarial extension of the tumour was also observed, although it was much more dramatic. Although the meningioma most likely induced the skull osteolysis reported here, it is important to mention the presence of the presumed adenocarcinomatous metastasis in this case, which might also have played a role in the lytic process. Indeed, other tumour types or pathological conditions inducing skull osteolysis have been reported in dogs and cats, such as squamous cell carcinoma,[14] choroid plexus carcinoma,[15] glioma,[16] pulmonary adenosquamous carcinoma metastases,[17] skull osteomyelitis[18] and intracranial epidural tuberculoma.[19]

In human medicine, osteolysis associated with intracranial meningiomas is a very rare finding and might be related to type 2 matrix metalloproteinase (MMP) expression. MMPs are proteolytic enzymes able to breakdown basal membranes and connective tissues.[20] Osteolytic changes are also reported in primary extradural intraosseous meningiomas, which represent <2% of human meningiomas overall.[21] Interestingly, in human, as in veterinary medicine, the majority of previously described osteolytic meningiomas have been benign, and osteolysis was not associated with a poorer outcome.[9–13,20,22] Nevertheless, although the meningioma described in the present report was not histologically very aggressive, it seemed to display a rather malignant behaviour. To our knowledge, there is no other case report of such an extensive osteolysis associated with a meningioma, in either human or veterinary medicine.

Another interesting feature of this case was the presence of the previously mentioned presumed metastatic adenocarcinomatous inclusions within the meningioma. In human and veterinary medicine, the presence of a tumoral entity inside another one may refer to three different concepts: collision tumours, tumour growth within another tumour and tumour-to-tumour metastasis (TTM).

Collision tumours consist of two or more distinct neoplastic lesions developing at the same location and which collide into one another.[23] In human medicine, this type of phenomenon is extremely rare, with approximately 30 cases reported, and most commonly involves a meningioma with an astrocytoma.[23] In veterinary medicine, collision tumours are also extremely rare and mostly involve testicular tumours in dogs.[24] In cats, the collision of a lymphoma and a fibrosarcoma has also been reported.[25] In our case, the presence of an extracranial T2W hyperintense lesion in continuity with an intracranial T2W hypointense lesion could have been interpreted as two different types of co-existing tumours. However, the histopathological analysis of a representative sample including both parts of the lesion failed to identify two distinct tumours. The extracranial part of the lesion consisted of a band of fibrous/reactive tissue, while the intracranial component consisted of meningioma. For these reasons, the hypothesis of collision tumours seems unlikely in this case.

Another rare phenomenon in human and veterinary medicine is the development of a tumour within another. It is suspected that the recipient tumour is usually a type of neoplasm that provides an adequate nutritional, vascular and/or hormonal environment, thus promoting the internal development of another tumour.[26] Two canine case reports have described this phenomenon, both involving a lipoma, harbouring either a cutaneous mast cell tumour[24] or a cutaneous haemangiosarcoma.[26] In both cases, the hosted tumours were primary neoplasms instead of metastasis, which makes this phenomenon different from our case.

TTM is also an uncommonly described phenomenon throughout the human medicine literature, with <100 cases affecting the CNS.[27,28] To our knowledge, only two cases of TTM have been described in the veterinary literature: one of a right heart auricle haemangiosarcoma with mammary gland tumour metastasis,[29] and the second of a forebrain oligodendroglioma hosting prostatic adenocarcinoma metastasis.[30] In people, meningioma represents the most frequent recipient tumour with TTM phenomenon affecting the CNS.[31] This higher incidence could be explained by various factors. Meningiomas are characterised by their rich vascularisation, low metabolic activity, hormonal factor expression and contain cell–cell adhesion molecules. All these characteristics may provide an appropriate environment for the development of metastasis.[28,31] In humans, breast and lung carcinomas seem to be the most common metastases-originating tumours participating in the TTM phenomenon.[28,32] The diagnosis of TTM is based on several criteria: (1) more than one primary

tumour must exist; (2) the recipient tumour must be a true neoplasm; (3) the metastatic neoplasm should show established growth in the recipient tumour; and (4) tumours that have metastasised to the lymph nodes where malignant tumours already exist are excluded.[33] In our case, the origin of the primary carcinoma remains uncertain. A first source of the metastasis could have been the lesion observed in the right nasal cavity. Although histopathology was not performed, a study demonstrated that nasal neoplasia was associated with moderate-to-severe turbinate destruction in 100% cases and with a mass-like effect in 89% of cases,[34] as observed herein. In this study, CT had a sensitivity and specificity >80% in the detection of distinct chronic nasal diseases, including tumours. Although nasal tumours more commonly invade the forebrain directly,[35] metastatic nasal carcinomas to the brain have been reported in dogs.[36] A second source could be the left thyroid nodule, which could be consistent with a malignant tumour. Indeed, brain metastases from thyroid tumours, including carcinomas, have already been reported in two dogs.[37] Unfortunately, a definitive diagnosis could not be reached for these lesions, as a full necropsy could not be performed as the owners did not consent to the procedure.

Lastly, another hypothesis could be the occurrence of a metastatic carcinoma of unknown primary origin (MCUPO). The latter refers to a biopsy-proven malignancy in which the anatomical origin of the primary tumour cannot be detected after a thorough patient history, a careful physical examination and comprehensive ancillary tests.[38] In people, MCUPO is the seventh most frequently occurring type of cancer, representing 3–5% of all diagnosed malignancies.[39,40] Interestingly, this phenomenon has also been described in veterinary medicine, and carcinoma was the most frequently diagnosed type of tumour.[38]

Conclusions

This is the first case report of an intracranial meningioma associated with such an extensive calvarial osteolysis in veterinary medicine. This is also the first description of presumed metastatic adenocarcinomatous inclusions inside an intracranial feline meningioma – a rare phenomenon called TTM in people.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval The work described in this manuscript involved the use of non-experimental (owned or unowned) animals. Established internationally recognised high standards ('best practice') of veterinary clinical care for the individual patient were always followed and/or this work involved the use of cadavers. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*. Although not required, where ethical approval was still obtained, it is stated in the manuscript.

Informed consent Informed consent (verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (experimental or non-experimental animals, including cadavers) for all procedure(s) undertaken (prospective or retrospective studies). No animals or people are identifiable within this publication, and therefore additional informed consent for publication was not required.

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