Case Report

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Meningeal carcinomatosis and spinal cord infiltration caused by a locally invasive pulmonary adenocarcinoma in a cat

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Abstract

Case summary A 12-year-old domestic shorthair cat was presented with acute non-painful hindlimb proprioceptive ataxia localising to T3–L3 spinal cord segments. MRI revealed paravertebral muscular hyperintensity on T2-weighted images at the level of T7–T8 vertebrae. The cat improved on conservative management but deteriorated 3 months later. Repeated MRI showed meningeal enhancement at the same level and hyperintensity of the paravertebral musculature extending to the right thoracic wall and pleural space on short tau inversion recovery images. Thoracic CT showed mineralised lesions of the right lung, restricted pleural effusion and expansile bone lesions affecting multiple ribs. The cat had been treated for pyothorax 5 years earlier but manifested no current respiratory signs. Cerebrospinal fluid (CSF) examination showed lymphocytic pleocytosis but no neoplastic cells. Biopsy of the affected muscles and cytology of the lung and pleural lesions suggested a malignant epithelial cell tumour. Post-mortem examination confirmed a pulmonary adenocarcinoma locally infiltrating the thoracic wall, T7–T8 vertebrae and the spinal cord white matter. Meningeal carcinomatosis was detected with neoplastic cells invading the ventral median fissure of the spinal cord. No metastases were observed in other organs, indicating that neoplastic cells reached the spinal cord by direct extension.

Relevance and novel information Spinal meningeal carcinomatosis has not been reported in dogs or cats with extraneural tumours but is a well-recognised condition in humans. A metastatic cause of meningeal enhancement should be considered in patients with neurological signs of unknown origin. Imaging findings and CSF results can be non-specific.

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Introduction

Meningeal carcinomatosis (MC) is a rare complication of extraneural solid tumours, such as intestinal, mammary and cutaneous squamous cell carcinomas, and consists of a focal, multifocal or diffuse malignant infiltration of neoplastic cells in the leptomeninges of the brain and/or spinal cord.[1,2] Meningeal metastases can also be caused by central nervous system (CNS) tumours or haematological malignancies (leukaemic and lymphomatous meningitis)[3–5] and are with MC collectively described under the term neoplastic meningitis.[1] While MC has also been used in veterinary medicine to describe meningeal metastases caused by choroid plexus tumours,[3–5] this term is preferably reserved for extraneural tumours only in human literature.[6]

Reports of MC in dogs include carcinomas of mammary and colonic origin and one unidentifiable tumour, all associated with intracranial metastasis.[7–11] Choroid

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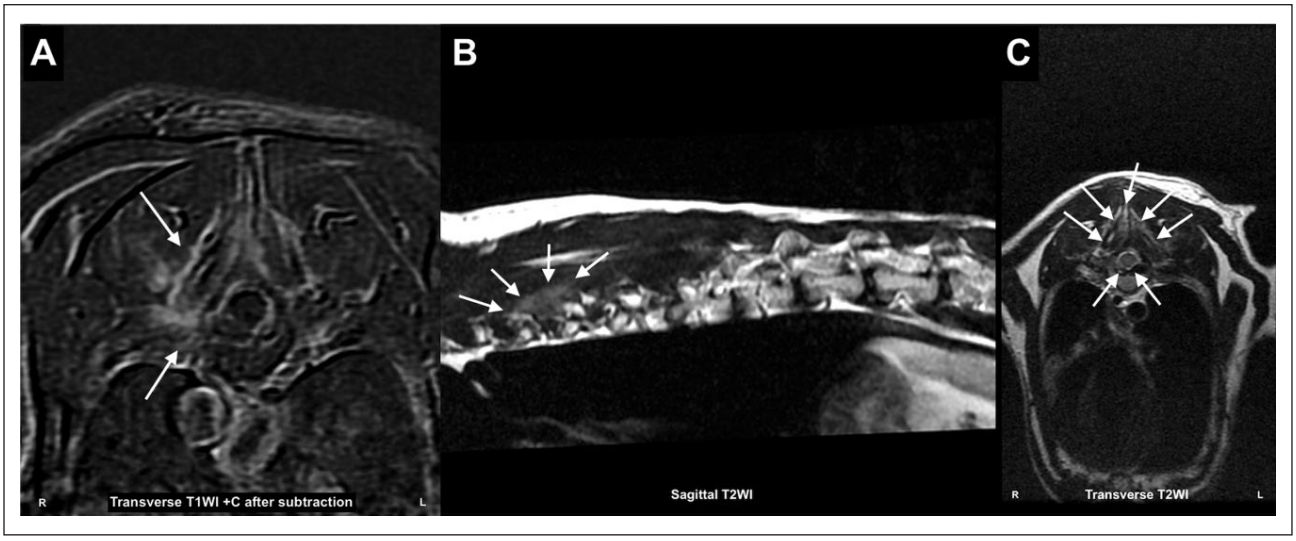

Figure 1 MRI findings on first presentation. (a) T1-weighted post-gadolinium subtracted image, paravertebral poorly demarcated contrast muscular enhancement (white arrows); (b) parasagittal T2-weighted image, paravertebral poorly demarcated muscular hyperintensity (white arrows); (c) transverse T2-weighted image, paravertebral poorly demarcated muscular hyperintensities and prominent vertebral venous sinuses at T7–T8 (white arrows)

plexus tumours have been reported to metastasise to the meninges of the brain and spinal cord in dogs but are not classified as extraneural tumours.[3–5] In cats, intracranial MC has been described in two cases with squamous cell carcinoma of the external ear.[12] In people, MC is a well-recognised condition occurring in 1–5% of patients with solid tumours. It is estimated that 5% of patients with breast cancer, 9–25% with small-cell lung cancer and 23% of patients with melanoma can develop MC.[1] The majority of these tumours present a pleomorphic distribution of leptomeningeal metastases in the CNS and around 60% affect the spinal cord and nerve roots.[1] In veterinary medicine, a choroid plexus carcinoma has been associated with both intracranial and spinal leptomeningeal metastases in a dog. However, spinal leptomeningeal metastases have not been described in dogs or cats with extraneural primary tumours.[5,8–12]

Case description

A 12-year-old neutered male domestic shorthair cat was presented out of hours with a 2 day history of acute non-painful hindlimb proprioceptive ataxia and mild ambulatory paraparesis localising to T3–L3 spinal cord segments. The cat had been treated medically for pyothorax 5 years earlier, having made a complete recovery and with no current respiratory signs. Physical examination was unremarkable and a basic biochemistry profile showed no abnormalities. An MRI scan (1.5 T) of the thoracolumbar spine was performed and revealed prominent vertebral sinuses at T7–T8 vertebrae with associated ill-defined extramedullary material of uncertain origin without causing spinal cord compression. Poorly demarcated paraspinal muscular hyperintensity on T2-weighted images (T2WI) and contrast enhancement especially visible on T1 subtraction images were also present at the same level (Figure 1).

Lumbar cerebrospinal fluid (CSF) analysis showed a mild mononuclear pleocytosis with mildly increased total nucleated cell count (12/µl) and elevated protein (107 mg/dl). CT of the chest and the abdomen was considered but declined by the client. While the final diagnosis remained open, a vascular or traumatic aetiology was suspected to cause the neurological deficits owing to the acute onset of the clinical signs. The cat was discharged on restricted exercise for 2–3 weeks, characterised by cage rest and avoidance of high-impact exercise. A telephone conversation 2 weeks later revealed that the cat remained non-painful and had shown a significant improvement.

The cat returned 3 months later with similar neurological deficits. The client reported that mild paraparesis had actually remained since presentation and recovery had been incomplete. The cat had been treated with meloxicam (0.05 mg/kg PO) intermittently and then once daily for the last 18 days. Haematology, biochemistry, urinalysis and blood pressure were unremarkable. MRI was repeated and showed no evidence of disc-associated lesion and the previously detected ill-defined material at T7–T8 was no longer visible. The prominent venous sinus remained similar in appearance. There was, however, evidence of a continuous area of T2 and short tau inversion recovery hyperintensity from the right thoracic region and dorsal pleural space to the paravertebral musculature in the cranial and mid-thoracic regions, with marked enhancement after gadolinium administration on T1-weighted images and T1 fat

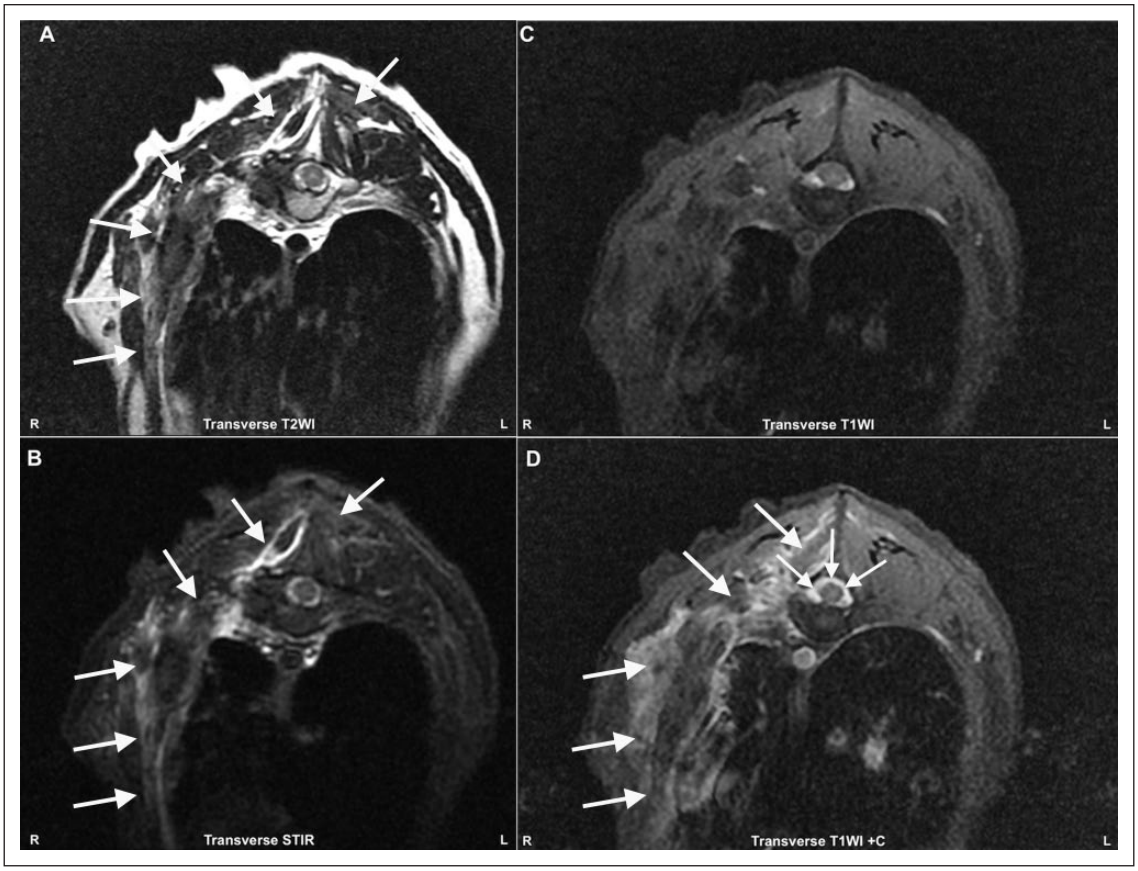

Fig 2 MRI findings on second presentation: (a) transverse T2-weighted image, prominent poorly demarcated hyperintensities extending from the right thoracic wall to the paravertebral tissues (white arrows); (b) transverse short tau inversion recovery image, prominent hyperintensities extending from the right thoracic wall to the paravertebral tissues (white arrows); (c) transverse T1-weighted fat saturation image and (d) transverse T1 fat saturation post-gadolinium image, marked contrast enhancement extending from the thoracic cavity and thoracic wall to the paravertebral tissues (white arrows) and marked circumferential meningeal enhancement (white arrows)

suppression images. The spinal cord at this level showed a very clear circumferential gadolinium enhancement of the meninges, which was not present in the first MRI scan (Figure 2).

Lumbar CSF examination showed genuine lymphocytic pleocytosis (total nucleated cell count 20/µl) and elevated protein (245 mg/dl) but no neoplastic cells. A CT (16-slice) scan of the thorax showed multiple mineralised consolidated lesions of the right cranial and middle lung lobe and lateral portion of the right caudal lung lobe causing parenchymal distortion and atelectasis with restricted pleural effusion and expansion of multiple ribs. The vertebrae were unremarkable, yet a multifocal paravertebral muscular enhancement was noticeable (Figure 3).

Fine-needle aspirations of the lung lesion were highly suggestive of a malignant epithelial cell tumour on cytology. A Tru-Cut biopsy of the thoracic musculature neighbouring the mass showed infiltrating neoplastic epithelial cells with cilia, suggestive of a metastatic carcinoma of respiratory epithelial origin. Lastly, a non-septic exudate was identified in the right pleural cavity likely secondary to the inflammatory process associated with the necrotic lung tumour and thoracic muscle lesions.

The patient deteriorated within 2 days after investigations despite treatment change to dexamethasone (0.15 mg/kg IV q24h) and buprenorphine (0.02 mg/kg IV q8h). Worsening of the paraparesis and urinary function and newly detected spinal pain lead to euthanasia. Postmortem examination confirmed the clinical diagnosis. A pulmonary adenocarcinoma locally infiltrating the thoracic wall, paravertebral musculature, T7 and T8 vertebrae, and the spinal cord was detected. Interestingly, MC was present with neoplastic cells invading the leptomeninges, the ventral median fissure and the dorsal median groove of the spinal cord (Figure 4). A small number of neoplastic cells was also observed in the leptomeninges of the caudal thoracic segments. Moderate dilation of myelin sheaths was seen in multiple locations, mainly within the ventral and lateral funiculi throughout the studied sections of spinal cord (T1–T13). Neither meningitis nor metastases in any other organs were observed,

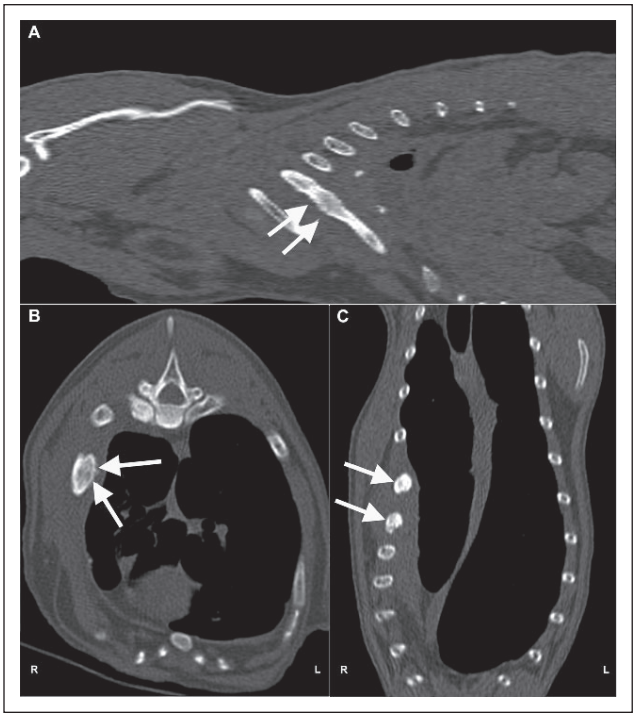

Figure 3 CT findings on second presentation: CT images of the chest, processed in bone algorithm, reconstructed with MPR (Multiplanar reconstruction) in (a) sagittal, (b) transverse and (c) dorsal planes. Sclerosis, thickening, remodelling and irregular periosteal reaction involving the VII and VIII ribs. The involved ribs (arrows) are the ones located in the vicinity of the pleural and pulmonary changes

indicating that neoplastic cells reached the spinal cord by direct extension.

Discussion

To our knowledge, spinal MC caused by direct extension of a pulmonary adenocarcinoma has not been reported in cats or dogs. The exact mechanism of how neoplastic cells can reach the leptomeninges in cases of MC is unclear.[1] Some of the publications in veterinary medicine describe a haematogenous dissemination,[8,12] and others include seeding of the CSF from choroid plexus tumours and encephalic metastases.[3–5,10] In human medicine, direct extension, haematogenous dissemination and spreading of the neoplastic cells along peripheral nerves and their lymphatics are the currently suggested routes of metastasis.[1] In the present case, the infiltration of neoplastic cells within the thoracic wall and paravertebral musculature, as well as vertebral bone marrow, together with the lack of metastases in any other organ, indicated that neoplastic cells reached the meninges and spinal cord by direct extension. This route has not been described for any of the reported cases with extraneural tumours causing MC in dogs or cats.[7–12]

Published veterinary MRI reports about MC are limited. Available publications describe dogs with neoplastic meningitis caused by choroid plexus tumours. Only one report was found to describe the MRI findings

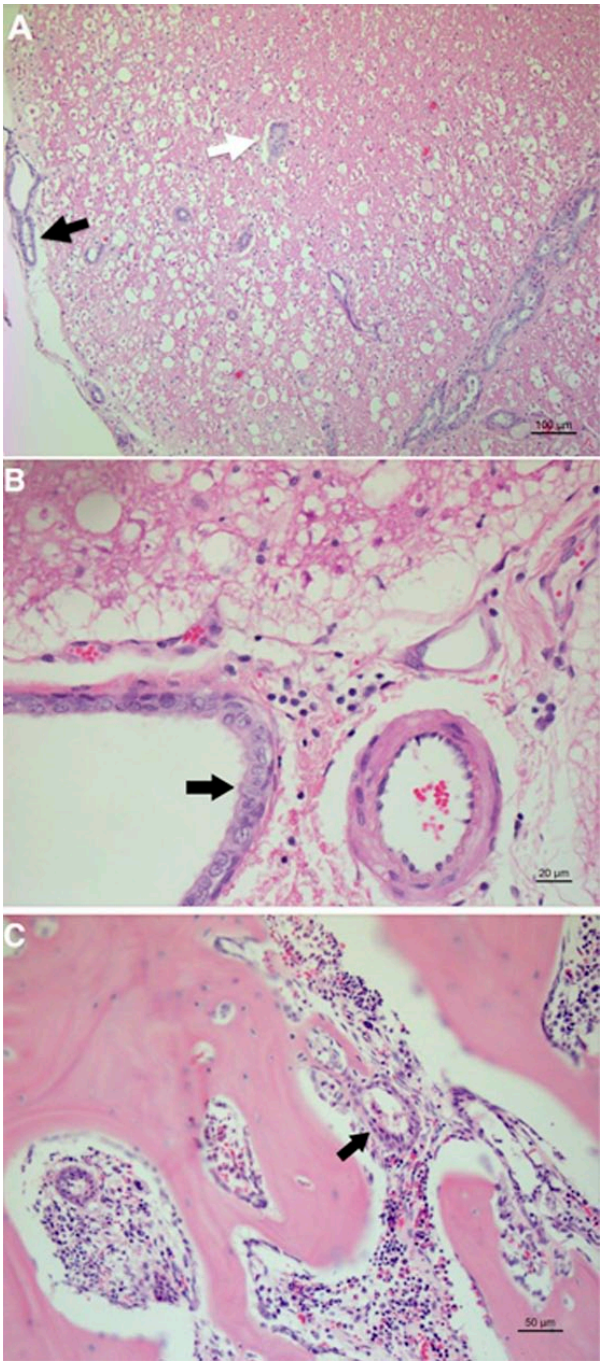

Figure 4 Histopathological features on post-mortem examination, haematoxylin and eosin staining: (a) multifocal aggregates of neoplastic epithelial cells forming tubules infiltrate the leptomeninges (black arrow) and white matter of the spinal cord (white arrow); (b) detail of cilia within the apical border of neoplastic cells infiltrating the spinal cord white matter (black arrow); (c) multifocal aggregates of neoplastic cells within the bone marrow of vertebral bone (black arrow)

in a dog with MC secondary to an extraneural (unidentifiable) tumour. Multiple extra-axial subarachnoid-enhancing lesions affecting the rostral and caudal fossae, together with cyst-like structures on T2-weighted and fluid-attenuated inversion recovery images, as well as T1-weighted widespread meningeal enhancement at the base of the brain were reported.[9] MRI findings of MC caused by defined extraneural neoplasms as seen in the here presented cat or in cats in general are not reported.[3–5] In people, meningeal contrast enhancement of the cortical convexities, basilar cisterns, tentorium, ventricular ependymal surface, cauda equina and/or cranial nerves are the main reported MRI findings of MC. Neoplastic disease of the leptomeninges can also appear as multiple intradural extramedullary enhancing mass lesions with or without hydrocephalus.[1]

Diagnosing MC can be challenging. It is suspected that MC and spinal cord infiltration were likely the cause of the existing neurological deficits on first presentation. MC is identified with contrast-enhanced MRI only in approximately 50% of affected human patients and meningeal enhancement is not generally present in early metastatic leptomeningeal disease.[1] Similarly, no meningeal abnormalities were detected on the first presentation in this cat. Such a disparity between MRI and histological findings is well known in veterinary medicine and it is described for inflammatory, neoplastic and vascular diseases.[13–16] The small degree of paraspinal muscular hyperintensities on T2WI on the initial MRI scan was unspecific and has been reported with inflammatory spinal cord disease,[17] spinal neoplasia,[18] paraspinal infection and myopathies,[19,20] as well as traumatic disease.[21] Meningeal contrast enhancement itself can also be unspecific and has been seen with infectious, inflammatory, traumatic or neoplastic diseases.[22] This demonstrates the necessity of performing more investigations for underlying primary non-neurological diseases in patients with neurological signs of unknown origin.

Interestingly, CSF analysis was not diagnostic in any of the two evaluated samples. Mildly increased cell count and moderate-to-marked elevation in the protein level were identified but are generally unspecific. These abnormalities can be seen in a variety of disease processes including spinal cord compression due to intervertebral disc disease, neoplasia, infection/inflammation, and traumatic or vascular aetiologies.[23–27] Neoplastic cells were not identified on CSF cytology, which is not unusual in cases of MC in human patients.[1] Reviewing archived CSF samples can increase the sensitivity of CSF cytology in identifying neoplastic cells that have been previously missed.[28] In people, additional tests are performed on CSF when metastatic disease is suspected. These include monoclonal antibody techniques, tumour-specific markers and flow cytometry.[1]

The final diagnosis of MC was made on histology. The post-mortem examination showed classical elements of MC characterised by infiltration of the leptomeninges with malignant carcinomatous cells presenting similar histopathological features and morphology, as seen in the primary lung tumour. Primary pulmonary neoplasia in cats is characterised by a high metastatic potential.[29] Local infiltration of the pleura, thoracic wall, paravertebral musculature, vertebrae, meninges and spinal cord, as part of the same metastatic process, has not been described in cats with primary lung tumours. In a study of 39 cats with pulmonary carcinomas, metastasis was present in 80% of cases at presentation, with decreasing order of intrapulmonary metastasis, intrathoracic carcinomatosis, regional lymph node infiltration and distant extrathoracic dissemination.[29]

Given the location of the neoplasia and the history of pyothorax, a potential influence of the chronic inflammation in the tumour development is speculated.[30] Cell proliferation, further recruitment of inflammatory cells and production of reactive oxygen species that cause DNA damage and inhibition of DNA repair are some of the pathological processes triggered by chronic inflammation. In these conditions, existent sub-threshold neoplastic cells can be promoted to neoplastic cells with no physiological growth control.[30] No respiratory signs were observed or reported by the client, but chronic fibrous pleuritis, as well as chronic bronchopneumonia with bronchiectasis and mineralisation, were found during the post-mortem examination.

Conclusions

MC can be a devastating complication of feline pulmonary carcinomas, with very poor prognosis and limited therapeutic options. This case report aims to alert clinicians that diagnosing MC can be challenging. Although rare, a metastatic cause of meningeal enhancement in patients with neurological signs of unknown aetiology should be considered even if there is a lack of supportive laboratory or imaging findings.

Reports about MC in animals are rare and the incidence of the disease, as well as the efficacy of specific diagnostic modalities, are yet to be established in veterinary medicine. Nevertheless, there is a degree of correlation between human and veterinary literature. MC in dogs and cats has been associated with primary tumours that are known to cause the same disease in people. A similar metastatic pathophysiological behaviour can be suspected in animals with these types of neoplasia. Consequently, screening for MC should be considered in patients with cancer with unspecific neurological signs.

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