Spinal ectopic choroid plexus papilloma in a cat

Joana Tabanez¹, Samuel Beck², Colin Driver¹,³ and Clare Rusbridge¹,⁴

Abstract

Case summary A 10-year-old male neutered Russian Blue cat was presented with a 2-month history of progressive non-ambulatory paraparesis. Spinal MRI revealed a well-demarcated, compressive intradural extramedullary mass at the level of T1 vertebra. The mass had subtle hyperintensity on T2-weighted images, was isointense on T1-weighted images and had diffuse, marked enhancement following gadolinium administration. Neuroaxis MRI, including limited brain sequences, excluded other visible lesions. Thoracic and abdominal radiographs were unremarkable. The mass was resected via a dorsal C7–T2 laminectomy and durotomy. Histopathology revealed a neoplasm composed of columnar-to-polygonal cells forming bilayered palisading patterns with a few apical cilia. Three mitoses were noted in 10 high-power fields. This was consistent with an epithelial neoplasm and initially a metastatic adenocarcinoma was considered most likely. Full-body CT with contrast and including the brain found rhinitis but did not identify any additional neoplastic foci. Biopsies of the nasal cavity and fine-needle aspiration of the spleen and liver were unremarkable. On immunohistochemical evaluation, pan-cytokeratin and E-cadherin immunolabelling was observed; however, synaptophysin, thyroglobulin, chromogranin A and glial fibrillary acidic protein was not detected. This, along with the histological morphology and absence of a primary tumour, was compatible with an ectopic choroid plexus neoplasm. Follow-up performed at 3, 14 and 24 months postoperatively revealed neurological improvement without recurrence.

Relevance and novel information We describe the presentation, histopathological and immunohistochemical features and outcome of a case of a rare ectopic choroid plexus neoplasm in the spinal cord of a cat.

Keywords: Extraventricular choroid plexus; atypical choroid plexus papilloma; surgical management; immunohistochemistry; cytokeratin; E-cadherin

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Case description A 10-year-old male neutered Russian Blue cat was presented with a 2-month history of right pelvic limb monoparesis that progressed to non-ambulatory paraparesis 2 days prior to presentation. Previous management included meloxicam (0.05 mg/kg q24h PO [Meloxaid; MiPet]), gabapentin (50 mg q12h PO) and acupuncture, to which there was no response. The general physical examination was unremarkable. On neurological examination, the cat was unable to walk with marked paraparesis. Postural reactions were absent on both pelvic limbs. Segmental spinal reflexes, mentation and cranial nerve examinations were considered normal, except for bilateral absent cutaneous trunci reflex. The neurological examination findings and clinical history were most compatible with a C8–T1 spinal cord segment lesion.

¹Neurology and Neurosurgery Department, Fitzpatrick Referrals Orthopaedics and Neurology, Eashing, UK
²VPG Histology, Horner Court, Bristol, UK
³Lumbry Park Veterinary Specialists, Alton, UK
⁴School of Veterinary Medicine, Faculty of Health and Medical Sciences, University of Surrey, Guildford, UK

Corresponding author: Joana Tabanez, DVM, MRCVS, Fitzpatrick Referrals Orthopaedics and Neurology, Halfway Lane, Eashing, Godalming, Surrey GU7 2OQ, UK
Email: JoanaT@fitzpatrickreferrals.co.uk
Haematology evaluation revealed moderate non-regenerative anaemia (packed cell volume [PCV] 23.9%, reference interval [RI] 30.3–52.3; red blood cells $4.53 \times 10^{12}$, RI 6.54–12.20). Serum biochemistry was unremarkable except for a marginal increase in glucose (9.22 mmol/l; RI 3.95–8.84) and globulins (52 g/l; RI 28–51). Feline leukaemia virus and feline immunodeficiency virus immunochromatography tests were negative. Survey thoracic and abdominal radiographs were unremarkable except for diffuse idiopathic skeletal hyperostosis at T11–L2, which was considered clinically irrelevant. The neurological findings indicated that MRI was appropriate. Sedation was performed using dexmedetomidine (2 μg/kg IV [Dexdomitor; Orion Pharma]) and buprenorphine (0.02 mg/kg IV [Buprenodale; Dechra]). General anaesthesia was induced with alfaxalone (5 mg/kg [Alfaxan; Jurox]) and maintained with isoflurane (Isoflo; Zoetis). MRI of the thoracolumbar spine was performed using a 1.5-T MRI unit (Siemens Symphony Tim system), which revealed a single, well-demarcated, suspected intradural extramedullary mass at the level of the T1 vertebra leading to marked dorsal compression of the spinal cord at that site. The mass lesion had a heterogeneous appearance, with a subtle patchy hyperintensity on T2-weighted sequences with a marked hyperintense core (Figure 1a,b) and was isointense on T1-weighted sequences with a hypointense core (Figure 1c,d). There was diffuse moderate paramagnetic contrast enhancement after gadolinium administration (0.1 mmol/kg [Dotarem; Guerbet Laboratories]) (Figure 1e,f). Images of the remaining neuraxis, including limited sequences of the brain, revealed no further lesions.

Differential diagnoses included meningioma, peripheral nerve sheath tumour, lymphoma and tumours of neuroectodermal origin. The owner elected for surgical biopsy and resection if possible. A dorsal approach to C7–T2 followed by a modified Funkquist type B dorsal laminectomy of the caudal portion of C7, entire T1 and part of T2, but preserving part of the T1 spinous process attached to the interspinous ligament and the T2 spinous process. Stay sutures were applied in the dura with 6-0 Vicryl (polyglactin 910; Ethicon), following a linear durotomy to allow identification and removal of the mass. There was a clear dissection plane between neoplastic and normal tissue. Haemostasis was controlled using Surgicel SNoW (Original Absorbable Hemostat; Ethicon) and routine closure was performed. No post-operative neurological deterioration was observed, and after 3 days of hospitalisation the cat was ambulatory with subtle paraparesis and proprioceptive ataxia. On discharge, manual PCV was 28% (RI 25–45).

Histopathological analysis revealed a well-demarcated, densely cellular, unencapsulated neoplasm arranged in tubules or acini, bilayered palisading patterns and packets, supported and subdivided by a fine fibrovascular stroma (Figure 2a). Neoplastic cells were columnar-to-polygonal, with moderate eosinophilic cytoplasm that contained a single round-to-oval nucleus. Nuclei contained a single nucleolus and stippled chromatin. There was mild anisokaryosis and anisocytosis (Figure 2b). Three mitoses were noted in 10 high-power magnification fields.
fields. The neoplastic population surrounded accumulations of eosinophilic proteinaceous fluid. A low number of cells exhibited fine apical cilia. Considering these features, an epithelial neoplasm of uncertain origin was suspected, compatible with a metastatic adenocarcinoma. Owing to apical cilia observed in neoplastic cells, a primary pulmonary neoplasm was suspected.

Following histopathological results, a full-body CT, including brain (160-slice Aquilion Prime; Toshiba), with ioversol contrast (2 ml/kg [Optiray 300; Guerbet Laboratories]) was performed in search for a possible primary tumour. Special attention was paid to epithelial sites such as skin, middle ear, lungs, intestine, kidneys, thyroid and anal glands. No mass lesion was identified, and the only additional pathologies recognised were a left nasal cavity destructive lesion; moderate hepatopathy with occasional hypoattenuating areas and marked splenic congestion. Biopsies of the nasal cavity were consistent with mixed neutrophilic–plasmocytic erosive rhinitis, with no evidence of fungal or neoplastic cells. Fine-needle aspiration of the spleen and liver were unremarkable.

Follow-up evaluation and neurological examination performed at 3 and 14 months revealed a subtle pelvic limb ataxia only.

The lack of clinical progression, failure to identify a primary tumour and prolonged survival time was considered highly unusual for a metastatic tumour. Hence, immunohistochemical evaluation of the excised mass was performed. The neoplastic population exhibited strong, fine-to-granular intracytoplasmic labelling for pan-cytokeratin in >90% of the neoplastic population (Figure 2c). No immunostaining was observed for synaptophysin, thyroglobulin, chromogranin A or glial fibrillary astrocytic protein (GFAP). Immunolabelling for E-cadherin was fine, mild-to-moderate, membranous and apical, consistent with an epithelial origin (Figure 2d). Given the absence of a primary neoplasm identification, positive immunolabelling for pan-cytokeratin and E-cadherin was considered supportive of a neoplasm arising from an ectopic choroid plexus.

At the 24-month telephone follow-up it was reported that the cat had returned to normal outdoor activity and had an excellent quality of life. The owner reported that they did not perceive the cat to have any neurological deficits.

Discussion
To our knowledge, this is the first report of a spinal choroid plexus tumour (CPT) in a cat. The choroid plexus
begins to form shortly after the closure of the neural tube, developing from invaginations of cells of mesenchymal and neuroepithelium origin.2,3 The choroid plexus epithelium originates from the roof plate at the sites of cerebral ventricle formation, developing sequentially as fourth, lateral then third ventricle.2–4 A layer of modified ependymal cells and one layer of vascular endothelium is organised in villous processes.4–6 The choroidal epithelial cells are cuboidal to columnar, with a central-to-basal nuclei and apical tight junctions. The cells have apical microvilli with projecting cilia and basal infoldings of the cell membrane, which have transcellular transport function.4,5

CPTs account for 10–12.8% of all primary brain tumours in dogs and are more often encountered on the fourth ventricle.7,8 In cats, however, CPTs have been rarely reported, with only one choroid plexus cystadenoma and one choroid plexus oncocytoma identified, according to the published literature.9,10

Histologically, CPTs resemble an exuberant version of the normal counterpart with branching papillary folds of cuboidal-to-columnar epithelium with microvilli, basal bodies and apical tight junctions.5,8,11 According to the World Health Organization (WHO) histological classification system for humans, CPTs are classified as grade I choroid plexus papilloma (CPP), grade II atypical choroid plexus papilloma and grade III choroid plexus carcinoma (CPC).12 Identification of atypical CPP is a segmental reaction to both low- and high-molecular weight cytokeratins.6,8,10,16,17 This specific epithelial feature separate CPTs from other neuroepithelial neoplasms.17 CPTs can variably express GFAP, mostly negative or minimally positive.6,16–18 The identification of GFAP immunostaining in CPTs might be explained by the close relationship between choroid plexus and ependymal cells. E-cadherin, cell adhesion molecules and β-catenin connecting protein are commonly expressed in canine CPT, regardless of grade.13,18 Reginato et al13 reported that N-cadherin immunolabelling is a more frequent feature of grade I tumours than high-grade tumours. Absence of N-cadherin expression has also been associated with the dissemination of CPCs within the neuroaxis.19 Human CPTs can also express S100, vimentin, epithelial membrane antigen (EMA), transthretin and rarely synaptophysin.8 Nuclear immunoreactivity for Ki-67 is a suggestive predictor of malignant behaviour and therefore of CPC.13,15 Kir7.1 has been reported as an excellent specific immunomarker for CPTs in dogs and useful in differentiating from metastatic carcinoma.14,20

In this report, the neoplasm presented cytokeratin immunolabelling but no GFAP immunomarking, indicative of a neoplasm of epithelial origin.16 The absence of labelling for chromogranin A, synaptophysin and thyroglobulin led to the exclusion of a neuroendocrine origin, including thyroid neoplasm. Differential diagnoses were ependymoma, CPTs and metastatic carcinomas. Previously described brain ependymomas in cats were characterised by the presence of perivascular pseudo rosettes or, less commonly, true rosettes.21 According to these reports,6,8,21 ependymomas presented variable positive immunolabelling for GFAP and absent-to-rare labelling with pan-cytokeratin antibodies. Nevertheless, ependymomas that do not express GFAP have been reported in dogs and cats, as have feline ependymomas that express rare pan-cytokeratin.21,22 According to Figarella-Branger et al,23 ependymomas do not express E-cadherin. Analysing all these reports regarding GFAP

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### Table 1 Choroid plexus tumour grading system in dogs (according to Westworth et al7)

| Histological grade | Mitotic figures per 10 HPFs | Other histological features |
|--------------------|----------------------------|-----------------------------|
| Grade I CPP        | <2                         | Minimal cell changes and invasion |
| Grade II ACPP      | 2–10                       | May also include up to two of the following features: increased cellularity; nuclear atypia; loss of papillary pattern or multilayered papillae; and areas of necrosis |
| Grade III CPC      | 5–10                       | At least four of the following morphological criteria: >5 mitoses per 10 HPFs; nuclear atypia; multilayered epithelium; increased cell density; loss of papillary pattern with solid cell growth; and/or multifocal areas of necrosis |

HPF = high-power field; CPP = choroid plexus papilloma; ACPP = atypical choroid plexus papilloma; CPC = choroid plexus carcinoma
and cytokeratin immunostaining, an ependymal origin was considered less likely along with the absence of rosettes or pseudorosettes and the presence of a fibrovascular rather than glial core. E-cadherin expression throughout the neoplastic population was consistent with an epithelial origin, which – when considered alongside the strong cytokeratin reaction – was supportive of a neoplasm arising from choroid plexus.\(^{18}\) Despite not having performed Ki-67 and/or Ki.7.1 immunolabelling, the tumour’s benign characteristics were reinforced by the exclusion of a clinically metastatic carcinoma by advanced imaging. Further, the survival time recorded in this case was inconsistent with a metastatic epithelial neoplasm.

According to the WHO histological grading system, this neoplasm was likely to be an atypical choroid plexus papilloma human counterpart, given the mitotic count (>2–10 high-power fields) and the bilayer of stratified epithelium.\(^{12,14}\) Subarachnoid seedings from primary intraventricular CPTs, also known as drop metastases, are not unusual in dogs.\(^{7,24–26}\) To our knowledge, these have never been reported in cats. As MRI and brain CT showed no evidence of an intraventricular mass, this neoplasm was considered to be of ectopic origin.

Ectopic CPTs in the spinal cord without intracranial mass lesions are exceptionally rare and scarcely reported in humans.\(^{27–29}\) Extramedullary thoracolumbar and sacral CPC with lung metastasis, intradural sacral nerve roots CPP and extradural S1–S3 CPP were reported as primary tumours without intracranial lesions in humans.\(^{27–29}\) An ectopic choroid plexus presacral cyst and two cases of intramedullary ectopic normal choroid plexus have also been described.\(^{30–32}\) Contrary to what might be expected, ectopic sites seem to be more common in adults than in children.\(^{33}\) This was interesting given the cat was 10 years old, but further conclusions could not be made as there are no reports of this type of tumour in cats.

The aetiology of ectopic spinal choroid plexus neoplasia remains unknown. It has been suggested to originate from dorsal midline mesenchymal-derived epithelial tissue that would normally invaginates into the developing brain after neural tube closure but, in this instance, inadvertently invaginates into subarachnoid space of the spinal cord during embryogenesis.\(^{2,32}\) The hypothesis of the choroid plexus epithelium arising by metaplasia from ependymal rests has been suggested as an alternative aetiology.\(^{28,29}\)

Surgical treatment of spinal cord or sacral ectopic choroid plexus or ectopic CPT in humans is associated with neurological improvement and no reoccurrence within a follow-up period of 3 months to 3 years.\(^{28–32}\) No further chemotherapy or radiotherapy treatment was provided in the above-reported cases. A poor prognosis was associated with ectopic choroid plexus carcinoma with metastasis.\(^{27}\)

In dogs, intracranial ectopic choroid plexus cyst without ventricular communication have been described.\(^{34,35}\) In a dog treated surgically, there were no signs of reoccurrence after 18 months.\(^{34}\) Similarly to the reported outcomes in both humans and one dog, this cat had no immediate neurological deterioration and no evidence of relapse at 24 months postoperatively.

In this case report, histopathological and immunohistochemical findings, together with the absence of a primary intraventricular CPT or other primary epithelial tumour, were suggestive of the first report of spinal ectopic choroid plexus papilloma in a cat. The long-term outcome of 24 months with neurological improvement adds to these findings.

**Conclusions**

This case report outlines a challenging diagnosis of spinal ectopic choroid plexus papilloma without a primary intracranial neoplasm. The importance of immunohistochemical evaluation aligned with histological growth pattern were crucial to the characterisation and differential diagnosis of this neoplasm, which was reinforced by survival time without reoccurrence.

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**Ethical approval** This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards (‘best practice’) of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not specifically required for publication in *JFMS Open Reports*.

**Informed consent** Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animal(s) described in this work (either experimental or non-experimental animals) for the procedure(s) undertaken (either prospective or retrospective studies). For any animals or people individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

**ORCID** Clare Rusbridge [10](https://orcid.org/0000-0002-3366-2110)
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