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Small intestinal peripheral nerve sheath tumour in a cat

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Abstract

Case summary A 5-year-old female spayed Chinchilla cat presented with a 4 week history of weight loss and inappetence. A thorough clinical investigation confirmed the presence of a distal jejunal mass. Histopathological and immunohistochemical analysis was consistent with a small intestinal peripheral nerve sheath tumour.

Relevance and novel information To the best of our knowledge, this is the first reported case of a small intestinal peripheral nerve sheath tumour in a cat. This case report demonstrates the use of immunohistochemistry in differentiating this entity from other mesenchymal neoplasms. The veterinary literature available in this field is very limited and this report adds a new differential diagnosis to feline patients presenting with an intestinal mass.

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Introduction

Peripheral nerve sheath tumours (PNSTs) consist of a heterogeneous group of neoplasms arising from Schwann cells, perineurial cells and fibroblasts, which represent the main elements of the endoneurium, perineurium and epineurium, respectively.¹

PNSTs are uncommon in domestic animals, being reported most often in dogs and cattle, infrequently in cats and horses and rarely in other species such as goats, pigs and birds.² Although PNSTs in animals most frequently occur in the peripheral nerves, cranial nerves and spinal roots, they may occur at other locations.³ In comparison with human medicine where recognition of PNST variants (eg, schwannoma, neurofibroma and neurofibrosarcoma) is important for management and prognosis, in veterinary patients the classification of these tumours is inconsistent and currently PNSTs are simply divided into benign and malignant based on cell morphology and invasiveness.¹

Information regarding PNSTs in cats is limited. Most previously reported cases are of PNSTs found in the skin, mainly in the area of the head, neck or limbs.^{4–6} They have also been described on the thoracic area, back, tail, flanks, perineal area and ischial area.⁵ Less common locations include periocular tissues,^{7–9} spinal canal,¹⁰ perirenal area¹¹ and urinary bladder.¹²

To our knowledge, this is the first case report describing a PNST arising in the gastrointestinal tract of a cat.

Case description

A 5-year-old female spayed Chinchilla cat was referred for investigation of a 4 week history of weight loss and inappetence. Preliminary investigations at the referring veterinary practice revealed an intra-abdominal mass of unknown origin.

On physical examination, the cat was bright and alert. Body condition score was 2/9. Clinical examination identified a 1.5 cm palpable intestinal mass within the mid-abdomen. A complete physical examination was otherwise unremarkable.

Further investigations were performed to determine the cause of the cat's weight loss and to investigate the origin of the intra-abdominal mass. Haematology and serum biochemistry were within normal limits. Abdominal ultrasonography identified a 14 mm eccentric intramural mass in one of the small intestinal loops. The mass was hypoechoic, heterogeneous and appeared

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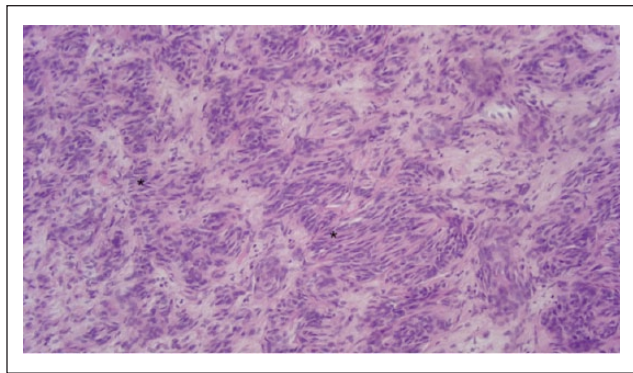


Figure 1 Histological appearance of the tumour; neoplastic spindle cells are arranged in short bundles, occasionally with nuclear palisades (asterisks). Haematoxylin and eosin stain ($\times 20$ magnification)

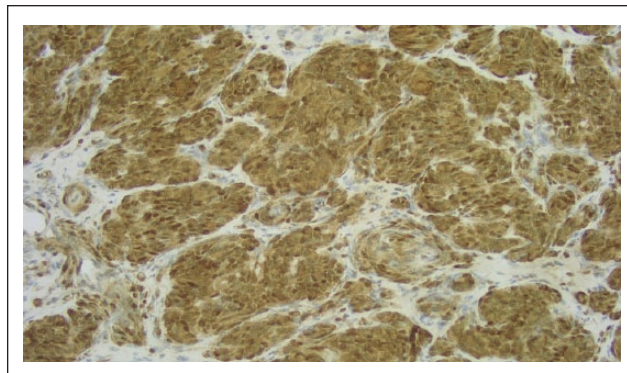


Figure 2 Positive immunohistochemical staining of neoplastic cells for S-100 ($\times 20$ magnification)

to arise from the intestinal muscularis layer. The mass was not causing an obstructive pattern, but focal distortion of normal wall layering was identified directly adjacent to the mass. The remainder of the small intestine had an altered wall layering with prominent submucosal and muscularis wall layers. Ultrasonographic abdominal examination was otherwise unremarkable. Fine-needle aspiration of the intestinal mass was performed. Cytological assessment on two occasions identified poorly cellular samples and was therefore considered non-diagnostic.

An exploratory coeliotomy was performed for diagnostic and therapeutic purposes. Surgical evaluation identified diffuse thickening of the ileum and confirmed the presence of a 1.5 cm mass on the antimesenteric border of the distal jejunum. This was resected with a 3 cm cranial and 2 cm caudal margin. An end-to-end anastomosis was subsequently performed. One mesenteric and one ileocecolic lymph node were also identified to be enlarged and excisional biopsies of these lymph nodes were performed.

A portion of proximal ileum and distal jejunum, including the jejunal mass, and two mesenteric lymph nodes were submitted for histopathological examination. The samples were routinely processed for histopathology and stained with haematoxylin and eosin. Histological evaluation of the distal jejunum revealed a non-capsulated, poorly demarcated and focally infiltrative neoplasm localised in the tunica muscularis with compression of the adjacent submucosa. The mass was composed of spindle cells arranged in short bundles, occasionally with a storiform pattern and nuclear palisades (Figure 1). These cells had poorly defined borders, scant eosinophilic fibrillar cytoplasm and elongated nuclei with finely stippled chromatin and 1–2 poorly visible nucleoli. Anisocytosis and anisokaryosis were mild to moderate. Mitoses were four in 10 high power fields.

Surgical margins were free of neoplastic cells. Based on the storiform pattern, nuclear palisading, infiltrating growth and mitotic count, a malignant PNST was suspected, but owing to the anatomical location a well-differentiated leiomyosarcoma and a gastrointestinal stromal tumour were also included in the list of the differential diagnoses.

Immunohistochemistry confirmed the diagnosis of PNST as neoplastic cells were diffusely and strongly stained by S-100 (polyclonal rabbit antibody, 1:800) (Figure 2) and glial fibrillary acidic protein (polyclonal rabbit antibody, 1:2000) (Figure 3), and negative for c-KIT (polyclonal rabbit antibody, 1:300) and smooth muscle actin (monoclonal mouse antibody, 1:100).

The mucosa of the proximal ileum and distal jejunum in proximity of the surgical margins was examined according to the World Small Animal Veterinary Association Gastrointestinal Standardization guidelines,¹³ and moderate lymphoplasmacytic mucosal inflammation was diagnosed. The mesenteric lymph nodes were reactive with follicular hyperplasia.

The cat recovered uneventfully and was discharged 72 h after the procedure. Further adjuvant treatment for the intestinal neoplasia was not pursued as it was completely excised. A hypoallergenic or novel protein diet was recommended for the following 6–8 weeks owing to the inflammatory changes documented in the proximal ileum and distal jejunum on histopathological examination. At the time of writing, the cat had no clinical signs (6 months after the initial diagnosis).

Discussion

To our knowledge, this is the first report of a PNST in the intestine of a cat. The diagnosis of PNST is usually based on histology, with or without immunohistochemistry.

Histologically, PNSTs are often characterised by the presence of Antoni A pattern (parallel arrangement of

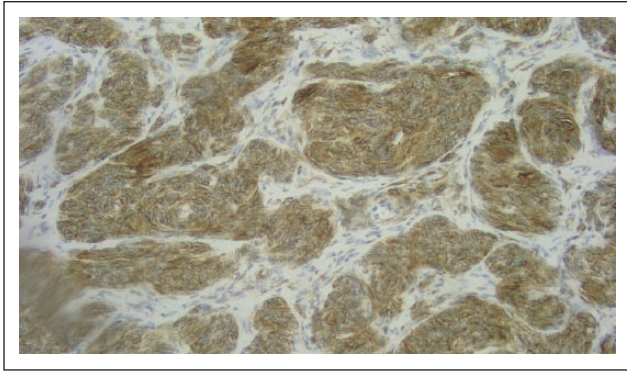


Figure 3 Positive immunohistochemical staining of neoplastic cells for glial fibrillary acidic protein ($\times 20$ magnification)

Schwann cell fusiform nuclei with a palisaded pattern with or without the presence of Verocay bodies) and/or Antoni B pattern (loosely arranged, hypocellular mixtures of Schwann, fibroblast and perineurial cells in a myxoid matrix), although these are not always visible, especially in malignant forms.^{5,14} The storiform pattern and nuclear palisading, which were noticed in the present case, are also considered suspicious of PNST, although these features are not specific and can be occasionally seen in other spindle-cell neoplasms. Owing to the lack of convincing Antoni A and Antoni B patterns, immunohistochemistry was used in this case to confirm the neural origin (glial fibrillary acidic protein positivity and S-100 positivity) and rule out other possible spindle-cell tumours of the small intestine such as gastrointestinal stromal tumour (c-KIT negativity) and leiomyosarcoma (smooth muscle actin negativity).

This PNST was histologically classified as malignant based on the infiltrating growth and mitotic count, according to previous studies.^{5,6}

The human classification into subtypes of PNST (eg, schwannoma, neurofibroma and neurofibrosarcoma) based on the presumed cell of origin is not usually applied for diagnostic purposes in veterinary medicine as the histogenesis is more uncertain and detailed information on the biological behaviour of these subtypes in animals is missing.^{5,6}

In the present case, the intestinal location of the PNST was considered unusual. Most PNSTs in cats are localised on the skin, although a few other anatomical locations have been reported.^{5,7,10,11} Feline PNST can be locally invasive, but they usually do not metastasise.⁵ Even if the metastatic rate tends to be low in these types of tumours, they more commonly metastasise through the haematogenous route rather than lymphatic system. In this case the local lymph nodes were removed owing to their macroscopically abnormal appearance to exclude fully metastatic disease; however, full staging with thoracic radiography was not possible. In a study performed

on 53 cats with PNSTs involving skin, subcutis, skeletal muscle and/or mucous membranes, 20% of the animals had local recurrence more frequently with histologically malignant tumours than with histologically benign tumours.⁵ Only one case of metastatic disease has been documented in the feline species and this was a maxillary PNST that spread to the regional lymph node and lung.¹⁵ PNST involving internal viscera in cats has been very rarely reported with only one case described affecting the urinary bladder.¹² The exact behaviour of this tumour could not be established in this report.

In the intestine of cats the most common neoplasm is lymphoma, followed by adenocarcinoma and mast-cell tumour.¹⁶ All of these neoplasms can have variable ultrasonographic appearances, but they can show as eccentric intramural mass as in this case. A focal inflammatory lesion was considered less likely with the ultrasonographic appearance of the lesion, but could not be fully excluded prior to histopathological assessment. Feline non-lymphoid mesenchymal intestinal tumours are rare and spindle-cell tumours, in particular, are extremely uncommon. There are a few case reports, case series and epidemiological studies in which intestinal fibrosarcomas and leiomyosarcomas have been reported in cats.^{15,19,20,21} In general, the prognosis with feline intestinal leiomyosarcoma is unclear owing to the small number of reported cases.¹⁹

Gastrointestinal PNSTs have been reported in dogs and horses.^{2,22–24} The two cases documented in the canine species were classified as benign PNSTs based on histopathological characteristics; however, the treatment, prognosis and follow-up in these dogs were not described. In two of the horses, the prognosis was good after surgical resection of the tumours and histologically they were classified as a neurofibroma of low malignancy in one of the cases and multiple benign PNSTs in the other case.

PNSTs are well recognised in humans and these are usually associated with a disease called neurofibromatosis type 1 (NF-1, or Von Recklinghausen's disease). NF-1 is an autosomal dominant disorder caused by a mutation in the NF-1 tumour suppressor gene and characterized by the formation of multiple neurofibromas in the skin, subcutaneous tissues, cranial nerves, spinal root nerves and, occasionally, in the gastrointestinal tract. Rare cases of gastrointestinal PNST not associated with NF-1 have also been described.²⁵ Malignant PNSTs (MPNSTs) are the malignant counterparts to benign soft tissue tumours, such as neurofibroma or schwannoma, and they have also been rarely associated with NF-1.²⁶ The prognosis of MPNST in humans seems to depend on many factors; however, MPNST is thought to have a far worse prognosis than other soft tissue sarcomas, because of its high likelihood of producing local recurrence and distant metastasis. Because of its low incidence, the optimal

treatment of MPNST is not fully established, but like other soft tissue sarcomas, only the complete surgical resection can provide the chance for cure.²⁷

In the case described here, wide surgical excision of the PNST was performed and no adjuvant treatment was pursued owing to complete excision. The patient was started on hydrolysed protein hypoallergenic diet or novel protein diet given the suspicion of concurrent inflammatory bowel disease based on the degree of inflammation found on ileal and jejunal biopsies. One limitation of this case report is the short follow-up available in this case and the incomplete staging provided that thoracic radiographs were not performed before or after the surgery owing to financial constraints. Repeat abdominal ultrasound 6 months after the surgery was recommended; however, this was declined. The cat remained without clinical signs up to 6 months after the procedure; however, the cat was lost to follow-up after this time.

Conclusions

This case report demonstrates that PNST should be considered in the differential diagnosis for intestinal spindle-cell neoplasia in the cat. Histopathological analysis and immunohistochemistry are useful in differentiating PNSTs from other similar entities such as gastrointestinal stromal tumours and leiomyosarcomas. Prognosis and prediction of biological behaviour remains challenging given the lack of accurate classification of these tumours in veterinary medicine.

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