A rare case of cecal malignant peripheral nerve sheath tumor in a dog

Hyerin AHN1,2, Woo-Jin SONG1,2*, Solji CHOI1, Jae-Hoon KIM2,3, Ji-Youl JUNG2,3, Jongtae CHEONG2,4, Hyunjung PARK2,5, Hyoohon JEONG1,2, Youngmin YUN1,2

1) Laboratory of Veterinary Internal Medicine, College of Veterinary Medicine, Jeju National University, Jeju, Korea
2) Research Institute for Veterinary Medicine, College of Veterinary Medicine, Jeju National University, Jeju, Korea
3) Laboratory of Veterinary Pathology, College of Veterinary Medicine, Jeju National University, Jeju, Korea
4) Laboratory of Veterinary General Surgery, College of Veterinary Medicine, Jeju National University, Jeju, Korea
5) Laboratory of Veterinary Imaging, College of Veterinary Medicine, Jeju National University, Jeju, Korea

ABSTRACT. A 12-year-old mixed-breed dog presented with a 2-month history of abdominal distension. Radiographic examination, abdominal ultrasonography, and computed tomography revealed a mass in the cecum (15.0 × 11.9 × 4.5 cm). The cecal mass was surgically removed and examined histopathologically. Immunohistochemically, the neoplastic cells expressed S-100 and neuron specific enolase but not α-smooth muscle actin and CD117 (c-kit). These histologic and immunohistochemical features indicated that the mass was consistent with a malignant peripheral nerve sheath tumor (MPNST). In dogs, most MPNSTs arise from the brachial plexus, spinal nerve root, and skin of the extremities. However, gastrointestinal MPNSTs in dogs have not been described previously. To the best of our knowledge, this is the first report to describe cecal MPNST in a dog.

KEYWORDS: cecal mass, dog, gastrointestinal mass, immunohistochemistry, malignant peripheral nerve sheath tumor

A 12-year-old 5.6 kg neutered male mixed-breed dog was presented to the Veterinary Medical Teaching Hospital, College of Veterinary Medicine, Jeju National University in the Republic of Korea with a 2-month history of abdominal distension. Physical examination revealed a body condition score of 4/9, and the abdomen was markedly distended. The biochemical profile and complete blood count were normal. On the radiographic view, a large, round, soft tissue opaque mass was visualized in the ventral abdomen, and it was difficult to make the evaluation of the dorsocaudal part of the abdomen (Fig. 1). Abdominal ultrasonography revealed a large, heterogeneous echotexture mass (Fig. 2). Ultrasound-guided fine-needle aspiration of the abdominal mass revealed low cellularity and mesenchymal cells. Preoperative and post-contrast-enhanced computed tomography of the abdomen was performed for surgical planning. A soft tissue-attenuating large mass (15.0 × 11.9 × 4.5 cm) was noted within the middle of the abdomen. A segment presumed to be the cecum was embedded from the back to the inside of the mass, which had relatively distinct margins (Fig. 3).

An exploratory laparotomy was performed for diagnostic and therapeutic purposes. The dog was premedicated with 0.2 mg/kg intravenous midazolam (Bukwang Midazolam; Bukwang Pharm, Seoul, Korea) and anesthetic induction was achieved by injecting 6 mg/kg propofol (Anepol; Hana Pharm, Seoul, Korea) intravenously; it was maintained with isoflurane and oxygen (1.5–1.8% concentration of isoflurane in oxygen). A large, firm, and well-circumscribed round cecal mass weighing approximately 1.6 kg (approximately 28% of the body mass) was surgically resected (Fig. 4A) and submitted for histopathology. The samples were routinely processed for histopathology and stained with hematoxylin and eosin. The mass consisted of a papulation of neoplastic spindle cells present in the interwoven bundle that formed a herringbone pattern (Fig. 4B). Neoplastic cells exhibited hyperchromatic nuclei, and mild nuclear pleomorphism. Mitotic figures counted in 10 high power fields (2.37 mm²) (diameter of the field of view = 0.55 mm; 40 objective and 10× ocular field number (FN) 22 mm; BX43 microscope, Olympus, Tokyo, Japan) were 0–1. Immunohistochemically, the neoplastic cells were positive for S-100 (DAKO, Hovedstaden, Denmark) and neuron specific enolase (NSE; DAKO) and negative for α-smooth muscle actin (α-SMA; DAKO) and CD117 (c-kit; DAKO). Based on these histopathologic and immunohistochemical features, the mass was diagnosed as a malignant neoplasm of peripheral nerve sheath origin (Fig. 5A–D). The dog was discharged from the hospital 9 days postoperatively. Further adjuvant chemotherapy and recheck ultrasonography for the cecum tumor were proposed but declined by the owner. The dog remained well for more than 400 days, however, died 478 days after surgery due to tumor recurrence.

*Correspondence to: Song W-J; ssong@jejunu.ac.kr, Laboratory of Veterinary Internal Medicine and the Research Institute for Veterinary Science, College of Veterinary Medicine, Jeju National University, Jeju 63243, Korea

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Peripheral nerve sheath tumors (PNSTs) are generally classified as soft tissue tumors that usually arise from Schwann cells, perineural cells, fibroblasts, or other cells comprising the nerve sheaths. PNSTs may be subdivided into benign and malignant PNST (MPNST) variants [24]. Schwannomas and neurofibromas are the most common types of human benign PNSTs. Most MPNSTs in humans are localized in the trunk, head, neck, extremities, and paravertebral regions. [12, 24] MPNSTs of the gastrointestinal tract are rare [12]. Only 6 cases were observed to originate from the colon, and MPNST of the cecum has not been reported previously to our knowledge [17]. The relationship between MPNST and neurofibromatosis 1 (NF1) is well known in humans. Neurofibromatosis is an autosomal dominant disorder, and up to 50% of MPNSTs are associated with NF1. NF1-related MPNSTs reportedly have a worse prognosis than non-NF1-related MPNST [5, 6, 11, 25].

In dogs, most MPNSTs arise from the brachial plexus, spinal nerve root, and skin of the extremities [4, 8, 23]. Canine MPNSTs have also been reported in other uncommon sites, such as the liver, spleen, adrenal gland, bladder, and diaphragm [1, 7, 10, 14, 15]. Two cases of benign PNSTs in the gastrointestinal tract were reported previously [21]. However, gastrointestinal MPNSTs in dogs have not been described previously. To the best of our knowledge, this is the first report of MPNST originating from the cecum in a dog.

Gastrointestinal MPNSTs are rarely reported in cats, and only two cases have been reported to our knowledge [2, 18]. Ribas et al. reported a small intestinal MPNST without metastasis in a 5-year-old female spayed chinchilla cat that was treated with complete surgical excision. The cat remained free from clinical signs for up to six months [18]. Boland et al. described a colonic MPNST with hepatic metastasis in a 14-year-old male neutered domestic medium-hair cat that was treated with surgical resection and metronomic cyclophosphamide. The cat experienced recurrence, and post-mortem examination identified MPNST within the kidneys and liver 18 months postoperatively [2].
Histopathologic diagnosis of MPNST is often difficult because it is a diverse group of heterogeneous neoplasms [19, 20]. Immunohistochemistry is used to confirm the neural origin and exclude other possible spindle cell tumors. Although we could not perform immunohistochemistry using more neurologic markers such as nerve growth factor receptor, claudin-1, or nestin [7], expression levels of S-100 protein and NSE which are highly related to neural-derived neoplasia [8, 13] were evaluated in this study. In addition, different markers are used to exclude other possible non-angiogenic, non-lymphogenic intestinal mesenchymal tumors [13]. α-SMA and desmin are used to rule out smooth muscle tumors, whereas CD117 (c-kit) and CD34 are used to rule out gastrointestinal stromal tumors [2, 8, 18, 20]. In this case, we observed positivity for S-100 protein and NSE and negativity for c-kit and α-SMA.

Current treatment of MPNST in humans is similar to that of soft tissue sarcomas (STS). Complete surgical excision with wide negative margins is treatment of choice [9, 16]. The role of adjuvant radiotherapy and chemotherapy remains controversial. However, postoperative radiotherapy is often recommended to improve local control, especially after incomplete resection. No randomized trials have assessed the efficacy of specific adjuvant chemotherapy in MPNST [5, 6, 16, 17, 24]. However, Kroep et al. compared chemotherapy for MPNST and other STSs and reported similar outcomes. The retrospective data from 12 pooled trials indicated that a doxorubicin-ifosfamide combination was associated with a lower risk of relapse and better response rate [9]. Wang et al. reported that a patient with multiple metastatic NF-1 related MPNSTs was administered combination chemotherapy with ifosfamide, carboplatin, and etoposide, known as ICE chemotherapy after the primary lesion was resected. It has been 12 years since his first visit, and he remains disease-free [25]. Chaudhary et al. described a case of a 10-year-old male dog with MPNST with NF-1 who achieved a complete response to metronomic therapy with etoposide, cyclophosphamide, and prednisolone [5].

Only a few instances of metronomic therapy as MPNST treatment have been reported for dogs and cats. Metronomic therapy with cyclophosphamide and piroxicam delays recurrence in dogs after incomplete surgical excision [3, 22]. In addition, in a cat with colonic MPNST treated with surgery and metronomic cyclophosphamide, clinical signs recurred 18 months postoperatively [2]. However, the optimal treatment for gastrointestinal MPNST remains poorly established due to its rare occurrence.

In conclusion, to our knowledge, this is the first reported case of cecum MPNST in a dog. The dog remained free of clinical signs for 12 months postoperatively without adjuvant chemotherapy.
CONFLICT OF INTEREST. The authors declare no conflict of interest with respect to publication of this manuscript.

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