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Gastrointestinal Autonomic Nerve Tumor in a Dog - A Case Record

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Abstract: This is the report of the histomorphologic and immunohistochemical features of a small intestinal tumor resembling human gastrointestinal autonomic nerve tumors (GANTs) in a seven-year-old male terrier dog. Grossly, the tumor mass, 8.0 × 4.0 × 6.5 cm, was cystic and enveloped the jejunum and had a white-gray color at cross section appearance. Histopathologically, long spindle-shaped cells arranged densely in a whorly pattern. The tumor cells had a low rate of mitosis, showed pleomorphism and, immunohistochemically, were positive for vimentin, α-smooth muscle actin, desmin,C-KIT, S100, GFAP and PCNA and negative for CD34. Then it can be a peripheral nerve sheath tumor resemble GANTs that originate from auerbaches plexius, because of C- KIT, GFAP and S100 expression.

Key words: Dog · Gastrointestinal autonomic nerve tumor · C- KIT · GFAP

INTRODUCTION

Gastrointestinal (GI) neoplasia, compared to neoplasia of other systems, occurs rarely in dogs. Most of GI tumors in dogs are not benign and tend to be invasive and metastasize. Small intestinal tumors are less malignant than large intestinal tumors [1]. In canine normal stomach and intestines criteria, the myofibroblasts near the crypts as well as muscles of the GI walls are SMA and desmin positive. Desmin expression is negative in gastrointestinal stromal tumours (GISTs) [2]. The myofibroblasts of gastric and intestinal tumours originate from fibroblasts which behave as stem cells and were named Interstitial Cajal Cells. Cajal cells are pacemakeric myofibroblasts, which GISTs originate from them [3]. GISTs, leiomyoma, leiomyosarcoma and schwannomas have the same histological features in HE staining [4, 5]. They are a heterogenous group of tumours immunohistochemically [6]. The most types of mesenchymal tumours in the GI of dogs are GISTs [1]. Immunohistochemically GIST-like tumours are the same as GIST but lacked C- KIT expression [7, 6, 1]. Desmin expression is very rare in GISTs [8]. Therefore, desmin negativity with presence of C- KIT is remarkable of differentiation of GISTs from myogenic or neurogenic tumours. C- KIT and CD34 are negative in schwannomas in spite of S100 protein which is almost positive. It is difficult to distinguish GISTs with S100 positivity (rare) f rom Schwannomas but schwannomas lacks C- KIT expression [4, 5]. Human gastrointestinal autonomic nerve tumours (GANTs) are the GISTs tumours which express neural markers [6]. The equivalent of GANTs in animals is peripheral nerve sheath tumours. In contrast of human GANTs which were not multicentric [9], peripheral nerve sheath tumours in the intestinal wall of a horse are multicentric [10]. GANTs were expressed S100, GFAP (glial fibrillary acidic protein) and desmin in humans as well as Peripheral nerve sheath tumours of a horse [10]. Myogenic (smooth muscle actin positive) as well as neurogenic (S100 positive) and/or undifferentiated mesenchymal elements can be related to animal peripheral nerve sheath tumours immunohistochemically [6].

The aim of this study was to firstly report the histomorphologic and immunohistochemical features of a small intestinal tumor resembling human gastrointestinal autonomic nerve tumors (GANTs) in a seven-year-old male terrier dog.

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MATERIALS AND METHODS

Tumour samples were formalin fixed and paraffin embedded (FFPE). Histologic sections (5 µm) were stained with hematoxylin and eosin (HE) and were also evaluated immunohistochemically for the expression of vimentin (V9, mouse monoclonal, dilution:1/50, Dako, Denmark), smooth muscle actin (1A4, mouse monoclonal, dilution: 1/50, Dako, Denmark), desmin (D33, Mouse monoclonal, dilution:1/50, Dako, Denmark), S-100 protein (polyclonal rabbit, dilution: 1/50, Dako, Denmark), GFAP(6F2, mouse monoclonal, dilution:1/50, Dako, Denmark), CD34(QBEnd 10, mouse monoclonal, dilution: 1/50, Dako, Denmark), C-KIT(CD117) (polyclonal rabbit, dilution: 1/50, Dako, Denmark) and proliferating cell nuclear antigen (PCNA) (PC10, mouse monoclonal, dilution:1/100, Dako, Denmark).

RESULTS

A seven-year-old male terrier dog was referred to the Clinic of the Faculty of Veterinary Medicine, with a ten-week history of vomiting and weight loss. The stomach, large intestines and kidneys appeared normal radiographically. The liver was slightly hepatomegalic. There was a large soft tissue mass effect in the center of the abdomen and the radiographic diagnosis was small intestinal tumour. She died among the surgery because of emaciation. A jejunal mass was revealed at necropsy that expanded the intestinal wall and peritoneum. The tumour mass, 8.0 × 4.0 × 6.5 cm, was cystic and covered the jejunum and had a white-gray color at cross section appearance (Figure 1). Microscopically, the tumor characterized by spindle cells in nodular whorls or streams and bundles (Figure 2), high nuclear to cytoplasm ratio, bizarrely shaped large hyperchromatic nuclei (Figure 3), without inflammatory component and necrosis. Mitotic rate was 1 per high-power fields (HPF). The immunohistochemistry of this dog tumour showed diffuse vimentine, SMA, desmin (Figure 4), S100, C- KIT, GFAP and PCNA (Figure 5) expression and no CD34 expression.

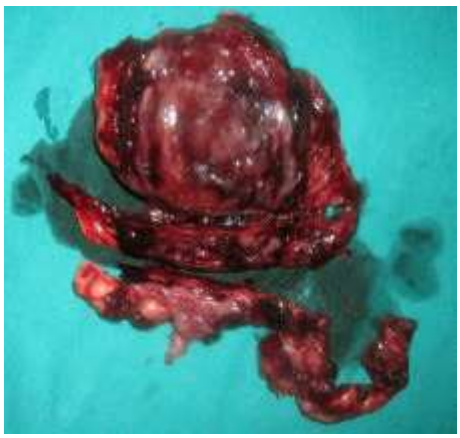

Fig. 1: Gastrointestinal autonomic nerve tumor; Dog. Tumor mass infiltrated the entire circumference of the intestinal wall and peritoneum

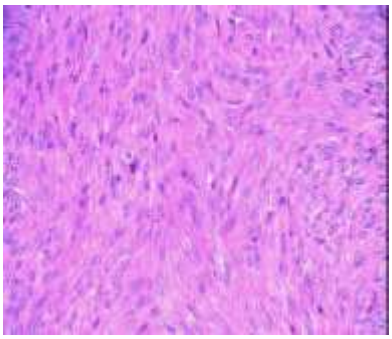

Fig. 2: Gastrointestinal autonomic nerve tumor, Dog. spindle cells in nodular whorls or streams and bundles, (H&E ×400)

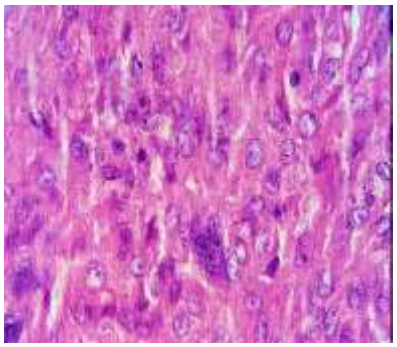

Fig. 3: Gastrointestinal autonomic nerve tumor, Dog. Bizarrely shaped large hyperchromatic nuclei, (H&E ×650)

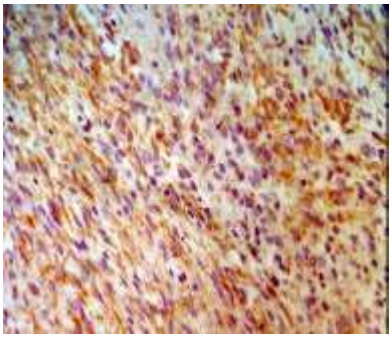

Fig. 4: Gastrointestinal autonomic nerve tumor, Dog. Diffuse desmin positivity (×250)

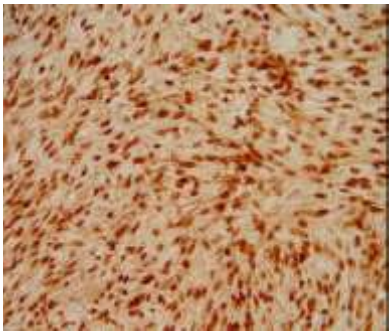

Fig. 5: Gastrointestinal autonomic nerve tumor, Dog. Diffuse PCNA positivity (×250)

DISCUSSION

This case showed overlapping immunohistochemical features between GIST and schwannoma. This is the report of the histologic and immunohistochemistric features of a small intestinal tumour resembling human GANTs in a dog. In contrast to describe animal peripheral nerve sheath tumours which were multifocal [6], in this case there was a large mass without any metastatasis in the other organs. This tumour was not schwannoma because of C-KIT and desmin expression, not leiomyosarcoma because of C- KIT and GFAP expression and not usual GISTs because of the simultaneous presence of desmin, GFAP and S100 and negativity for CD34. Then it can be a Peripheral nerve sheath tumours because of C- KIT, GFAP, desmin and S100 expression. The equine GISTs were well demarcated and no metastasis was noted [11]. In contrast, gastric stromal tumours described in nonhuman primates can metastasize [12]. In dogs, malignant GISTs are more commonly reported in the jejunum and cecum and are generally slow to metastasize [13, 14]. There is no correlation of PCNA expression with survival in GISTs [15]. The tumour of this case was not multicentric and in contrast of PCNA expression (Fgure 5) and pleomorphism, behaves as benign tumour without any metastasis to other organs.

We belief that evaluation of more canine GISTs leads to more detection of peripheral nerve sheath tumours that is necessary to better understand their frequency, specific features and pathogenesis that help to better treatment of this type of tumours.

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