

## Desmin expression by a gastrointestinal stromal tumor in a dog

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### Key Words:

Dog; gastrointestinal stromal tumor; C-KIT; desmin.

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### Abstract

This report describes the histological and immunohistochemical features of a small intestinal tumor that resembled a human gastrointestinal stromal tumor (GISTs) in a seven-year-old male cross-breed dog. This was unique because of the expression of desmin by the tumor. Grossly, the white-gray tumor measured 8.0 × 4.0 × 6.5 cm and was 760 gram in weight. It was cystic and enveloped the jejunum. Histopathologically, long spindle-shaped cells were arranged densely in the interwoven pattern. The tumor cells had a low rate of mitosis, were pleomorphic, and were positive for vimentin, -smooth muscle actin, desmin, S100 and C-KIT and negative for CD34 on immunohistochemistry. The expression of desmin in the cytoplasm of this tumor cells is a rare event in these types of tumors.

### Introduction

Gastrointestinal (GI) neoplasia occurs infrequently in dogs compared to the frequencies of neoplasia that involve other systems. Over two-thirds of GI neoplasms in dogs are malignant. They are aggressive and often spread locally or to other areas (Maas *et al.*, 2007). Cecal tumors had more histological malignancy than small intestinal tumors. In the normal canine stomach and intestines, SMA and desmin are demonstrated in pericryptal myofibroblasts and smooth muscle cells of the muscle layers (Mukaratirwa *et al.*, 2003). In contrast to SMA labeling, desmin labeling was negative in tumor stromal cells (in both gastric and intestinal tumors), except in regions of tumor close to the muscularis mucosa (Mukaratirwa *et al.*, 2003). This suggested that myofibroblasts in gastric and intestinal tumors originated from pre-existing fibroblasts, except in tumor regions close to the muscularis mucosa, where the myofibroblasts appeared to originate from smooth muscle cells of the muscularis mucosa (Mukaratirwa *et al.*, 2003). Gastrointestinal stromal tumors (GISTs) are proposed to originate from the interstitial cells (myofibroblasts) of Cajal, which are precursors to the pacemaker cells of the intestinal wall (Schmid and Wegmann, 2000).

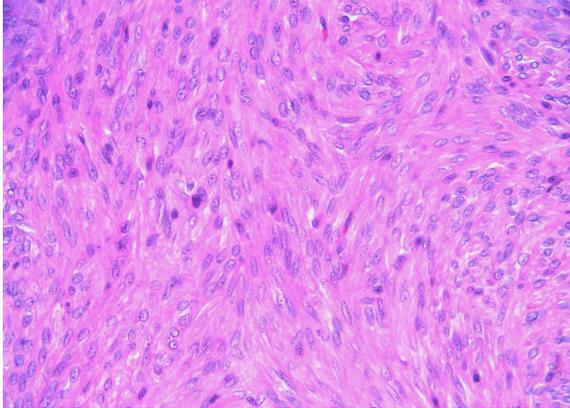
### Case Report

A seven-year-old male cross breed dog was referred to the clinic of the Faculty of Veterinary Medicine, University of Tehran, with a 10-week

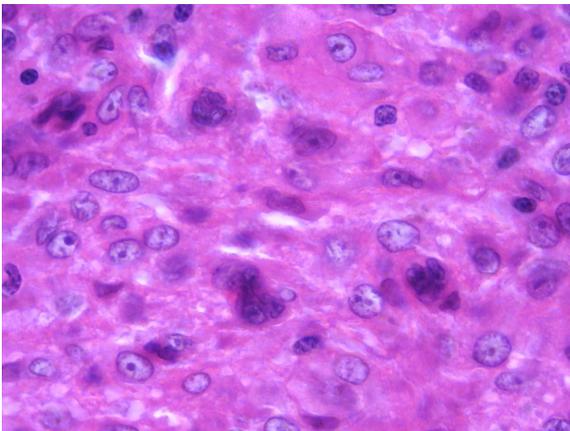
history of vomiting and weight loss. A radiograph was taken of its abdomen. The stomach, kidneys, large intestines, and bladder all appeared normal. The liver was slightly hepatomegalic. There was a large soft tissue mass effect in the center of the abdomen and the radiographic diagnosis was of a small intestinal tumor. He died after two days due to starvation and emaciation. Necropsy revealed a jejunal mass that had infiltrated the entire circumference of the intestinal wall and peritoneum. The tumor mass, which measured 8.0 × 4.0 × 6.5 cm, was cystic and enveloped the jejunum; it had a white-gray color at cross section appearance. Tumor samples were fixed in formalin and embedded in paraffin (FFPE). Histological 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), S100 protein (rabbit polyclonal, dilution: 1/50, Dako, Denmark), CD34 (QBEnd 10, mouse monoclonal, dilution: 1/50, Dako, Denmark) and C-KIT (CD117; polyclonal rabbit, dilution: 1/50, Dako, Denmark).

Microscopically, the mucosal surface was intact and not ulcerated, but the tumor had infiltrated and disrupted all of the intestinal layers, including the submucosa, muscular and serosal layers of the involved area. The tumor was characterized by spindle cells arranged in nodular whorls or streams and bundles (Figure 1), a high nuclear to cytoplasm ratio, and

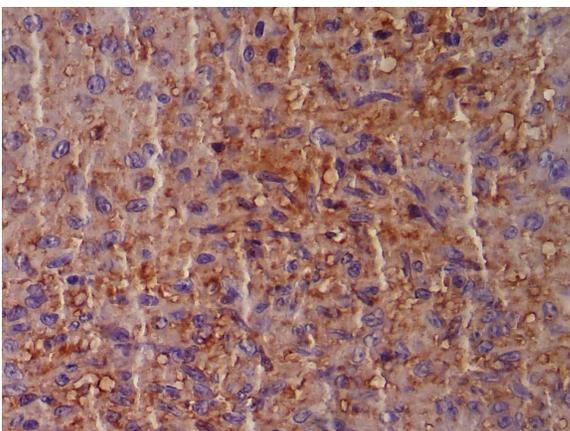
bizarrely shaped large nuclei (Figure 2), without an inflammatory component or necrosis. The mitotic count was 1 per each high-power field (HPF). The immunohistochemistry of this tumor showed patchy C-KIT (75%; Figure 3) expression, diffuse vimentin (100%), SMA (100%), desmin (75%; Figure 4) and S100 (65%; Figure 5) expression, and no expression of CD34 (Figure 6).



**Figure 1:** Gastrointestinal stromal tumor in the dog. Spindle cells in streams and bundles. (H&E x250).



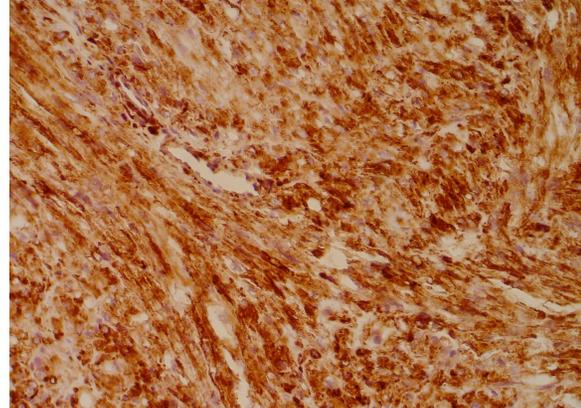
**Figure 2:** Bizarrely shaped large multilobulated nuclei in the GIST (H&E x750).



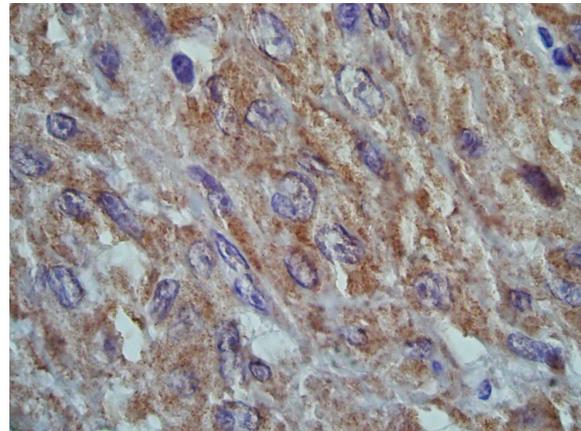
**Figure 3:** Expression of C-KIT in the cytoplasm of tumor cells.

## Discussion

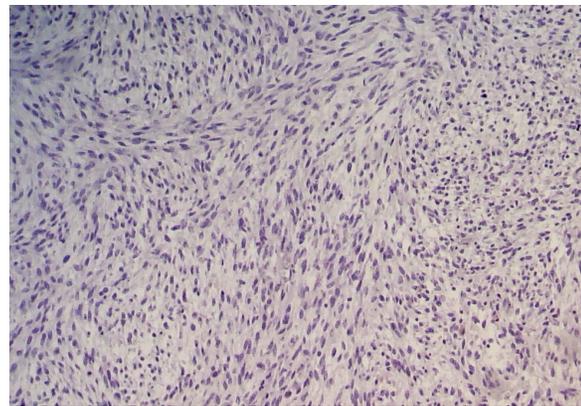
GISTs cannot be distinguished from smooth muscle tumors in HE-stained sections. It is plausible that GISTs represent stem cell tumors that can differentiate in to a Cajal cell-like or smooth muscle cell-like phenotype (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). GIST and GIST-like tumors in the small intestine of



**Figure 4:** Expression of desmin in the cytoplasm of tumor cells.



**Figure 5:** Expression of S100 in the cytoplasm of tumor cells.



**Figure 6:** No reaction of S100 protein antibodies in the cytoplasm of tumor cells.

dogs are the most types of mesenchymal tumors (Maas *et al.*, 2007). GIST-like tumors are similar to GIST without C- KIT expression immunohistochemically (Bettini *et al.*, 2003; Maas *et al.*, 2007; Cooper and Valentine, 2002). Desmin expression is very rare in GISTs. Therefore, the simultaneous lack of desmin and presence of C- KIT offers a sharp contrast between GISTs and true smooth muscle tumors for diagnostic purposes (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). Schwannomas are strongly positive for S100 protein and are always negative for C- KIT and CD34 (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). There were no tumors that showed overlapping features between GIST and schwannoma (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). The S100 positivity found in a small group of GISTs, especially those of small intestine, is intriguing (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). This observation is best explained by the multidirectional differentiation of these tumors, and the lack of C- KIT in schwannomas seems to allow for a sharp separation of GISTs and GI schwannomas (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003; Cooper and Valentine, 2002).

In this case, there was a large mass without any metastasis in the other organs and showed overlapping immunohistochemical features between GIST and either schwannoma or leiomyosarcoma. This tumor was not a schwannoma because of the C-KIT and desmin expression; furthermore, it was also not a leiomyosarcoma because of C- KIT and S100 expression, but it was not a typical GISTs because of the presence of desmin and S100 expression and negativity for CD34. Desmin expression rather than S100 is very rare in GISTs (Miettinen *et al.*, 2000; Miettinen and Lasota, 2003). Therefore, this tumor represents a rare form of GIST because of the simultaneous expression of C- KIT, S100 and desmin.

Equine GISTs are well-demarcated, and no metastasis from them has been noted (Hafner *et al.*, 2003; Cooper and Valentine, 2002). In contrast, gastric stromal tumors described in non-human primates can metastasize (Saturday *et al.*, 2005; Cooper and Valentine, 2002). In dogs, malignant GISTs are more commonly reported in the jejunum and cecum and are generally slow to metastasize (Kapatkin *et al.*, 1992; LaRock and Ginn, 1997). The tumor of this case was not multicentric and in contrast to its pleomorphism, behaved as a benign tumor without any metastasis to other organs. We believe that the evaluation of more canine GISTs in the future will lead to a better understanding of their frequency, specific features, and pathogenesis, which will assist in the more optimal treatment of this type of tumor.

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