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SHORT COMMUNICATION   Clinical Case Report

Neuromuscular and vascular hamartoma of the cecum in a dog

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Abstract

Neuromuscular and vascular hamartoma (NMVH) is a rare non-epithelial hamartoma of the intestine in humans that is characterized by proliferation of smooth muscle, blood vessels and bundles of unmyelinated nerve fibers in the intestinal submucosa. Here, we describe a case in which a mass lesion in the cecum of an 8-year-old male West Highland White Terrier dog. The mass caused an inversion of the cecum, which was surgically removed. The mass was found in the muscle layer of the inverted cecum, and on histology was composed of a proliferation of mainly spindle-shaped cells with fibrillar cytoplasm, vascular structures, and bundles of unmyelinated nerve fibers. These features of the mass are consistent with those described for NMVH in humans.

In humans, neuromuscular and vascular hamartoma (NMVH) is a very rare non-epithelial hamartoma of the intestine and only 24 cases have been reported[2,4,7]. In most of these cases, the NMVH was in the jejunum or ileum, and in one case in the cecum[7]. The clinical signs of NMVH in patients are usually non-specific abdominal pain, and symptoms of obstruction or occult chronic intestinal hemorrhage[2]. X-ray examination of the intestine of NMVH patients may reveal a stenosis, intussusception, or a polypoid mass[2]. Characteristic histologic findings include fascicles of smooth muscle derived from the muscularis mucosa, unmyelinated nerve fiber bundles with ganglion cells, and vascular structures with a thickened wall in the intestinal submucosa[2,4,7].

In most cases, a favorable outcome is achieved. However, cases of NMVH have not been described in veterinary medicine.

An 8-year-old male West Highland White Terrier was investigated for intermittent hematochezia. Ultrasonography revealed the so-called "target-shaped" sign in the intestines, and colonoscopy identified an intussusception of the inverted cecum into the colon. The inversion of the cecum was easily reducible by peristaltic motion.

The inverted cecum was surgically excised and examined. Macroscopically, the surface of the excised specimen was covered by cecal mucous membrane, due to complete eversion (Fig. 1A). When a cross-section of the inverted cecum was

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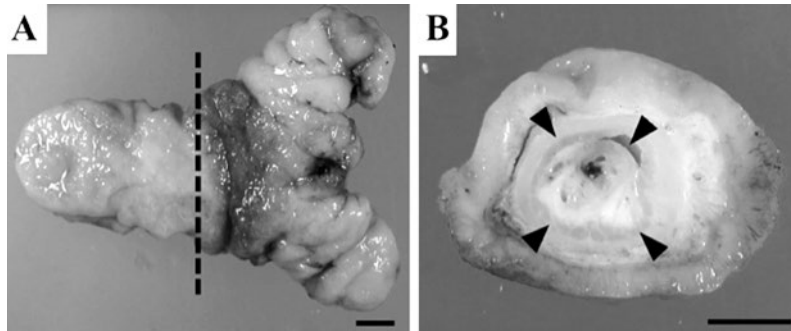TEL/FAX: +81-857-31-5422
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Fig. 1. The inverted cecum of the dog.
A: Gross appearance of the inverted cecum. The surface was covered by cecal mucous membrane due to complete eversion of the cecum. Cecal apex is left side, and cecal fundus is right side of the picture. B: Cross-section through the cecum at the broken line shown in A. An irregular mass lesion extends from the muscle layer to the serosa (arrowheads). Bars = 5 mm.
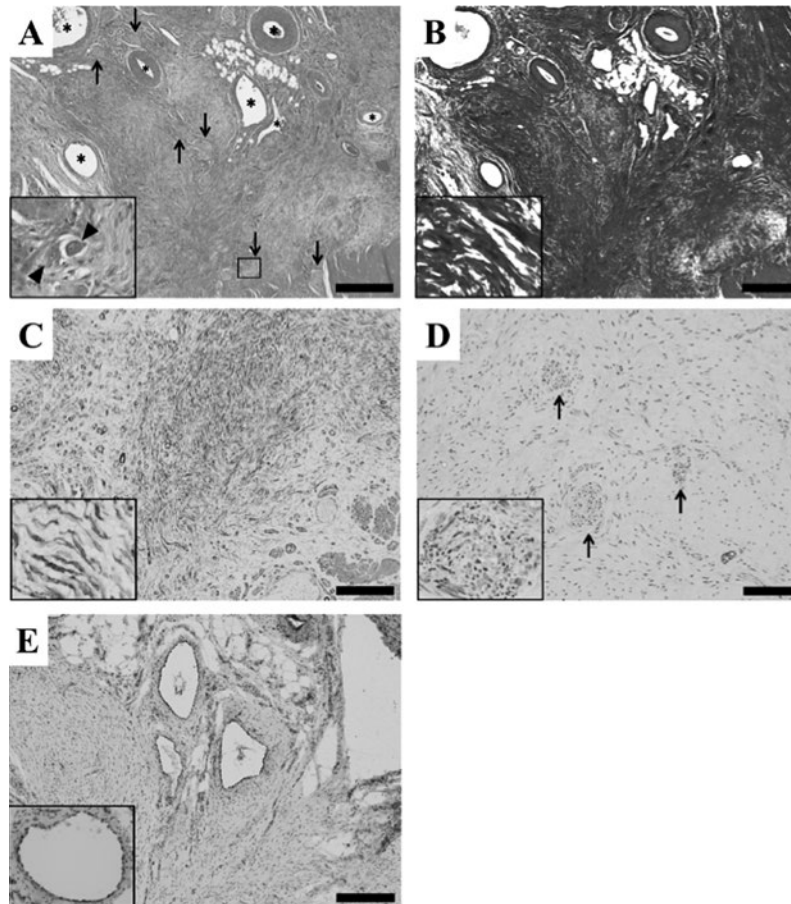

Fig. 2. Histology and immunohistochemistry of the mass found in the cecum of the dog.
A: Proliferation of spindle-shaped cells with fibrillar cytoplasm. In addition, many vascular structures (asterisks) that are dilated or have an irregularly thickened wall. Arrows show nerve fiber bundles. Magnified view of open square area showed in inset indicating ganglion cells by arrowheads. H&E. Bar = 500 μm. B: The fibrillar structures composed of a mixture of smooth muscle fibers (red) and collagen fibers (blue). Inset, higher magnification of fibrillar structures. Masson's trichrome staining. Bar = 500 μm. C: The spindle-shaped cells with fibrillar cytoplasm and artelioles are positive for α-SMA. Inset, higher magnification of positive spindle cells. Counterstained with hematoxylin. Bar = 100 μm. D: Bundles of unmyelinated fibers (arrows), immunostained with anti-neurofilament (NF) antibody and counterstained with hematoxylin. Inset, higher magnification of the bundle of positive fibers. Bar = 100 μm. E: Vascular structures that have irregular wall thickness, and vWF positive endothelium. Inset, higher magnification of the vessels. Counterstained with hematoxylin. Bar = 200 μm.
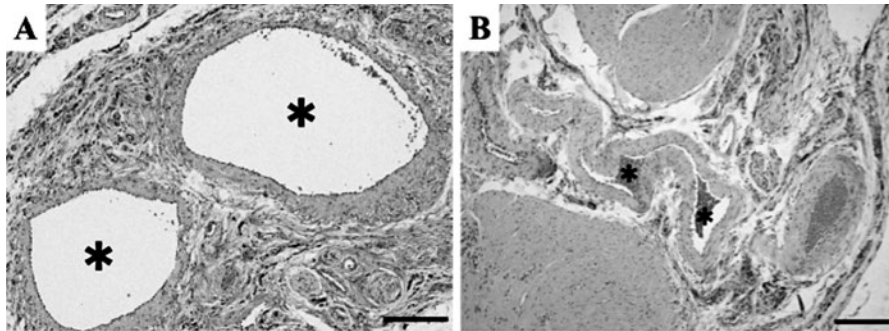
Fig. 3. The irregular vascular structures present in the cecal mass of the dog.
A: Dilated vascular structures (asterisks) with irregular wall thickness. Many small arterioles are also visible. H&E. B: Tortuous arteries (asterisks) within the mass. H&E. Bars = 200 μm.

examined, a whitish mass was identified that extended from the muscular layer to the serosa (Fig. 1B). The tissue was fixed in 10% neutral-buffered formalin, processed routinely, and embedded in paraffin wax. Sections (3-4 μm) were stained with hematoxylin and eosin (H&E) or immunohistochemically using antibodies targeting α-smooth muscle actin (α-SMA), von Willebrand Factor (vWF), or neurofilament (NF). Microscopically, the mass was composed of a proliferation of mainly spindle-shaped cells with fibrillar cytoplasm. In addition, vascular structures that were dilated or had irregularly thickened walls, and bundles of unmyelinated nerve fibers accompanied by ganglion cells were observed (Fig. 2A). Mitotic figures could not be identified in the cells. Masson's trichrome staining demonstrated fibrillar structures composed of a mixture of smooth muscle fibers (stained red) and collagen fibers (stained blue, Fig. 2B). Immunohistochemistry demonstrated labeling of the spindle-shaped cells with fibrillar cytoplasm with anti-α-SMA antibody, of the atypical vascular structures with both anti-α-SMA and anti-vWF antibodies, and of the unmyelinated nerve fiber bundles with anti-NF antibody (Fig. 2C-E). Many vascular structures were scattered throughout the mass, including arteries with irregular walls and following tortuous routes (Fig. 3). On the basis of these histologic and immunohistochemical findings, we concluded that the mass consisted of a proliferation of mainly smooth muscle

cells, bundles of unmyelinated nerve fibers, and atypical vascular structures.

Leiomyoma, leiomyosarcoma, and gastrointestinal stromal tumor are considered to be the major mesenchymal neoplasms of the lower gastrointestinal tract of domestic animals[8]. However, the histologic features in this case were different from those typically associated with the common neoplastic diseases, instead being consistent with those described for NMVH in humans[2,4,7]. According to previous literature, some cases of NMVH in human may be 'burnt out' form of Crohn's disease or another chronic inflammatory process[2,7]. In the present case, no histological finding of chronic enteritis were observed in the cecum. Infiltration of macrophages and lymphocytes (CD3 and CD20 positive lymphocytes by immunohistochemistry) were rarely seen, and silver staining (Grocott's staining) showed no pathogens on the specimen. Therefore, it is considered that the present lesion is not associated with chronic inflammatory diseases. Histology and immunohistochemistry showed that the mass removed from the present case was composed of smooth muscle cells, atypical vascular structures, and bundles of unmyelinated nerve fibers. The vascular structures consisted of capillaries and arteriovenous components with irregularly thickened walls. The nerve fibers of the myenteric plexuses were arranged normally in the inverted cecum, but many nerve fiber bundles were also present within the mass.

Therefore, we believe that nerve fiber bundles were elements of the mass, rather than normal myenteric nerves being involved in the formation of the mass. Accordingly, the mass was regarded as a hamartomatous lesion composed of a mixture of smooth muscle cells, vascular structures, and nerve fiber bundles, which are similar components to those of NMVHs in human patients[2,4,7]. In human NMVH, disorganized fascicles of smooth muscle cells are one of the features, whereas, in the present case, disorganized bundles of smooth muscle cells containing abundant cytoplasm were rarely seen. However, many blood vessels with unequal thickness walls as shown in Fig. 3, and dense presence of nerve fibers with ganglion cells within the mass are consistent with hamartomatous lesions. In addition, most lesions of NMVH in humans have been found the intestinal submucosa, meanwhile the present lesion was located in the muscular layer to serosa. These morphological differences might be related to species-specific variations between humans and dogs.

To date, few cases of NMVH have been reported in humans and none in animals. This may be because of the low incidence of NMVH, the difficulty of diagnosing this lesion, or the associated non-specific clinical signs or symptoms. The clinical presentations of patients with NMVH have been reported to be abdominal pain, obstruction, or occult chronic intestinal hemorrhage[2]. In the present case, there was intermittent hematochezia, a "target-shaped" sign on ultrasonography, and an inverted cecum detected using colonoscopy. The inverted cecum was surgically removed, and detailed pathologic examination revealed the presence of a mass in the muscle layer of the inverted cecum.

Cecal inversion is also a very rare intestinal disease, but has been reported in humans, dogs, cats, red wolves, and horses[1,3,5,6]. When the inverted cecum causes ileo-colonic obstruction, the clinical signs are chronic or intermittent bloody mucoid diarrhea, abdominal pain, and vomiting. In cases of complete obstruction, severe abdominal pain, vomiting, or depression has been recorded. Specific causes of inverted cecum in dogs have not been identified, but it seems that three important inciting factors may be involved in the formation of intussuscepta: anatomic intestinal border (duodenum-jejunum, ileum-cecum, or colon-rectum), mechanical compression, and abnormal peristaltic activity[6]. We speculate that the cecal inversion in this case was due to mechanical compression of the cecal wall by the mass. After surgery, the dog remained in good health, without any recurrence of clinical signs, for the following 9 months. To the best of our knowledge, NMVH has not been previously reported in an animal, but we provide evidence of its first identification here.

Acknowledgements

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