

Pathology in Practice

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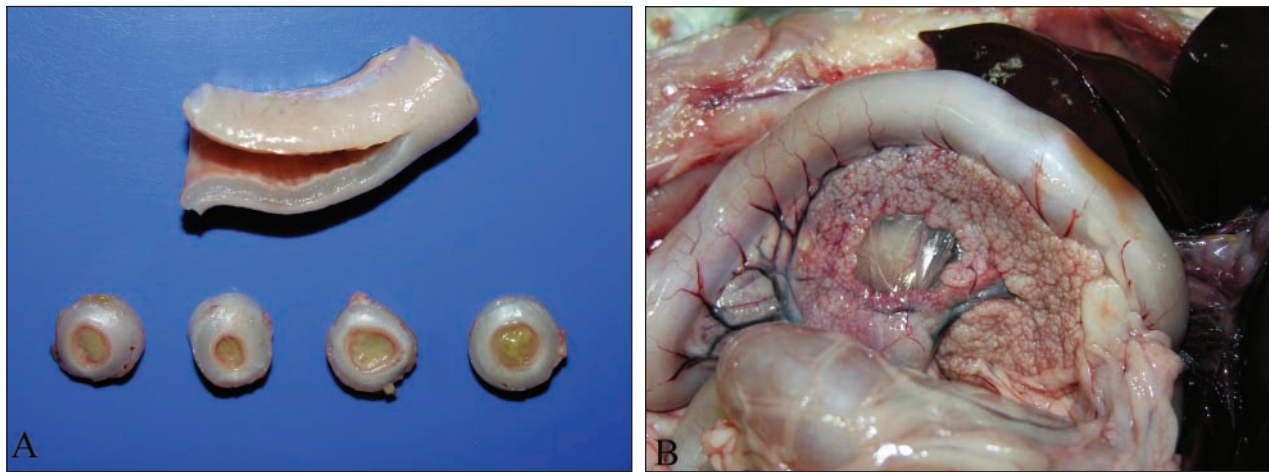
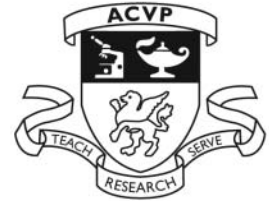


Figure 1—Photographs of portions of the small intestine (A) and pancreas (B) of a young female cat that had a 2-month history of chronic diarrhea and weight loss. In panel A, notice that the wall of the small intestine is concentrically hypertrophied (approx 4 to 6 mm in thickness). In panel B, the pancreas is diffusely pale, nodular, firm, and small.

History

An 8-month-old female domestic shorthair cat with a 2-month history of chronic diarrhea and weight loss was submitted for necropsy. A local veterinarian had treated the cat with pyrantel pamoate and metronidazole, but there was no response to treatment. The cat was also fed a low-residue diet without change in the clinical signs. During routine ovariohysterectomy, straw-colored fluid in the abdominal cavity and diffuse thickening of the intestinal tract were detected. Feline infectious peritonitis was suspected, and the cat was euthanized.

Clinical and Gross Findings

The cat was in fair body condition (body condition score, 2/5). Fleas were present on the coat.

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The cat's oral mucous membranes were pale, and there was mild hyperkeratosis of all foot pads. Yellow watery feces stained the perineal region, and the abdomen was distended. Necropsy revealed that the small intestine was rubbery in consistency, similar to a garden hose. The intestinal wall (duodenum to the ileocecal junction) was concentrically thickened; the thickness of the intestinal wall was 4 to 6 mm with moderate narrowing of the diameter of the intestinal lumen (Figure 1). The intestinal tract was filled with yellow mucoid to watery content. The jejunum had mild multifocal petechiae. The pancreas was small, pale, diffusely nodular, and firm. The mesenteric lymph nodes were abnormally large. On cut surface, the spleen had multiple, regularly distributed white foci, which were considered reactive lymphoid follicles.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

Histopathologic Findings

The walls of the duodenum, jejunum, and ileum were 4 to 5 times as thick as expected in a healthy cat. Histologic examination of sections of the small intestine revealed that the thickening was a result of hypertrophy of the tunica muscularis. Although both smooth muscle layers were involved, hypertrophy was most severe in the inner circular layer (Figure 2). Individual myofibers were enlarged with moderate amounts of eosinophilic cytoplasm and transverse hypereosinophilic bands (hypercontracted bands). Nuclei were abnormally large, vesicular, and elongated and occasionally had 1 nucleolus. Myofibers of the outer longitudinal layer were enlarged with mildly vacuolated cytoplasm. The glands were atrophic with collapse of the lamina propria and paucity of lymphocytes and plasma cells. In some sections, the glands were elongated because of goblet cell hyperplasia.

The pancreas had a diffuse nodular pattern as a result of severe interlobular and intralobular interstitial fibrosis and the presence of lymphoplasmacytic and neutrophilic infiltrates that dissected and replaced multiple pancreatic acini. Within lobules, moderate to severe acinar atrophy was characterized by depletion of zymogen granules and loss of acinar cells with replacement by mature fibrous connective tissue. The tunica muscularis around larger pancreatic ducts was mildly to moderately hypertrophied (Figure 3). Portal areas of the liver were infiltrated by mild to moderate numbers of neutrophils, lymphocytes, and plasma cells. The diffuse enlargement of the lymph nodes was due to severe lymphoid follicular hyperplasia.

Morphologic Diagnosis

Severe, diffuse small intestinal muscular hypertrophy; severe, chronic, fibrosing

and lymphoplasmacytic interstitial nodular pancreatitis with acinar atrophy and muscular hypertrophy of pancreatic ducts; and moderate, subacute, neutrophilic, lymphoplasmacytic portal hepatitis.

Comments

The gross and histopathologic findings in the duodenum, jejunum, and ileum of the cat of this report were typical of muscular hypertrophy of the small intestine (MHSI). Intestinal muscular hypertrophy along with potential maldigestion secondary to the severe fibrosing pancreatitis was the likely cause of the cat's chronic diarrhea and weight loss. Because the hepatic duct fuses with the pancreatic duct prior to entering the duodenum in cats,

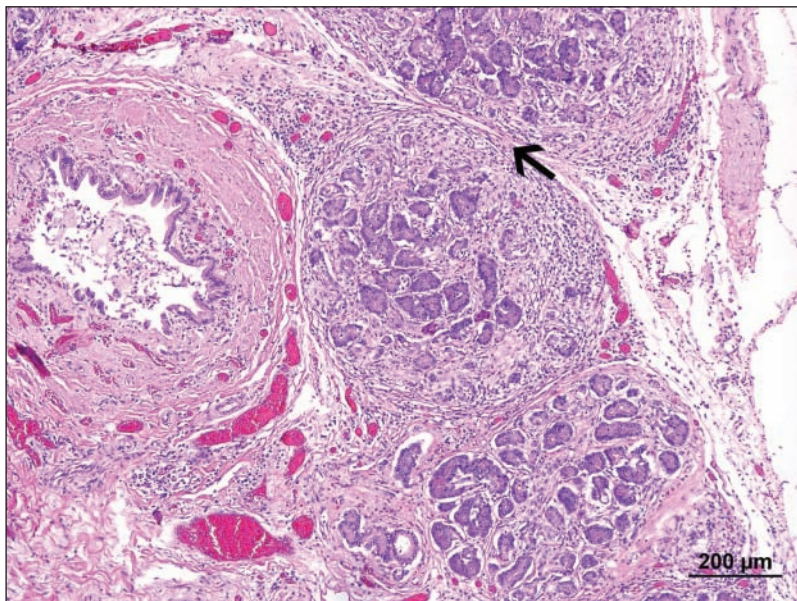


Figure 3—Photomicrograph of a section of tissue from the pancreas of the cat with MHSI in Figure 1. Notice that the interlobular septae (arrow) are expanded by fibrous connective tissue admixed with lymphoplasmacytic infiltrate. There is atrophy and loss of the pancreatic acini. Moderate muscular hypertrophy of the pancreatic duct wall is also notable. H&E stain; bar = 200 μ m.

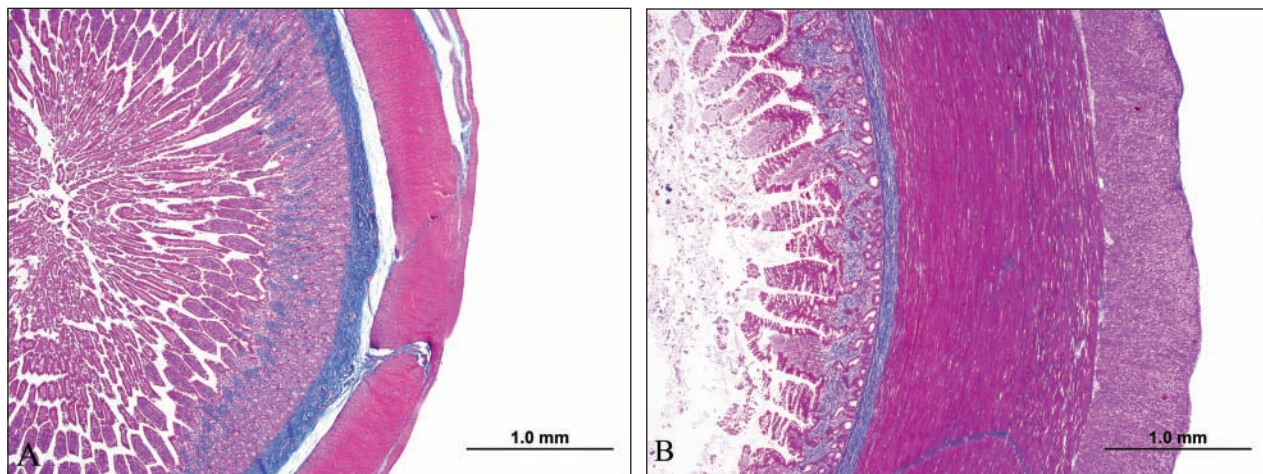


Figure 2—Photomicrographs of transverse sections of the jejunum from a cat that died (cause unrelated to gastrointestinal tract disease) and underwent necropsy (A) and from the cat with muscular hypertrophy of the small intestine (MHSI) in Figure 1 (B). Sections were obtained at the same anatomic location. In panel A, the thickness of the normal muscular layer (red) of the jejunum is evident. In the cat with MHSI, hypertrophy has resulted in a 4-fold increase in thickness of the muscular layer (primarily in the inner muscular layer). The lamina propria of the mucosa is collapsed with atrophy of the glands. In both panels, Masson trichrome stain; bar = 1 mm.

portal hepatitis and interstitial pancreatitis (as evident in the cat of this report) can be secondary to ascending infection (eg, in association with enteritis or inflammatory bowel disease).^{1,2} Smooth muscle hypertrophy of the pancreatic ducts might have contributed to the severity of the pancreatitis in this case. Pancreatic atrophy was most likely secondary to malabsorption associated with intestinal lesions and concurrent pancreatitis and fibrosis.

Muscular hypertrophy of the small intestine is considered primary or idiopathic if intestinal stenosis is not detected; it may also develop secondary to stenosis or partial intestinal obstruction (the compensatory form).^{1,3,4} Both forms have been identified in cats.^{1,4} The secondary (compensatory) form is usually segmental and has been linked with chronic enteritis, intestinal adenocarcinoma, alimentary lymphoma, or gastrointestinal parasitism.^{3,5} Grossly, alimentary lymphoma or other intestinal neoplasia should be considered as differential diagnoses, but associated luminal stenosis also could cause intestinal hypertrophy cranial to the neoplasia. The cat of this report appeared to have primary MHSI because no underlying cause was found.

Cats with MHSI typically have nonspecific and often chronic clinical signs that include anorexia, vomiting, and diarrhea; palpably thickened intestinal loops may be detected during physical examination.^{1,3} Ultrasonography is useful for diagnosing MHSI; findings are characterized by intestinal wall thickening with retention of apparently normal wall layering.³ At necropsy, wall width of the small intestine is increased and luminal narrowing is evident in cats with MHSI, compared with findings in unaffected cats.⁴ Histologically, hypertrophy is primarily present within the inner circular layer of smooth muscle of the small intestine and is not associated with smooth muscle inflammation or interstitial edema.^{3,4}

Primary (idiopathic) MHSI is a frequent finding in horses, commonly involving the ileum or extending diffusely throughout the entire small intestine.^{1,5,6} The distal third of the esophagus and cranial region of the nonglandular portion of the stomach may be also affected. Segmental or diffuse MHSI usually develops in mature horses (15 to 18 years old) with clinical signs of variable duration that include colic, intermittent diarrhea, and progressive weight loss.⁵ Although debatable, infection with *Anoplocephala* spp at the ileocecal orifice has been suggested as a cause of partial luminal obstruction that results in secondary intestinal hypertrophy in horses.^{1,5} In pigs, the terminal portion of the ileum is involved and MHSI may result in impaction and intestinal rupture; functional obstruction at the ileocecal orifice is thought to be the cause.¹ Of the 2 forms of MHSI, the pathogenesis of primary (idiopathic) MHSI is less understood. It is proposed that primary MHSI is neurogenic in origin and centered on an autonomic imbalance that results in uncontrolled peristalsis or prolonged spastic contraction of the ileocecal orifice.⁵

In the secondary form, at least 3 mechanisms may be involved: mechanical stretching, which increases smooth

muscle cell division and synthesis of contractile proteins; altered nerve discharge as a result of distension of the organ; and release of chemical factors that stimulate the muscle response. Secondary MHSI has been experimentally induced in rats and guinea pigs via surgical creation of a stenotic lesion; hypertrophy develops within 3 to 5 weeks.⁷ Thickening of the intestinal muscular layer has also been associated with experimental infection of rats with intestinal parasites.^{8,9} It has been hypothesized that secondary inflammation in response to the parasite infection causes increased synthesis of cellular proteins of smooth muscle cells, such as α - and γ -smooth muscle actins, in an attempt to increase contractility.^{8,9} It is believed that the main inflammatory cytokines involved in MHSI are interleukin-4 and interleukin-13, which are produced by T cells. These proinflammatory mediators are thought to act directly on muscle to increase contractility via signal transducer and activation of transcription factor-6-dependent mechanisms and induce hypertrophy through the induction of transforming growth factor- β .¹⁰

Muscular hypertrophy of the small intestine should be considered as a potential sequela to inflammatory bowel disease or infection and as a differential diagnosis in cases of segmental or diffuse alimentary neoplasia in mammals. For cats with signs of chronic anorexia, diarrhea, and weight loss, MHSI should be considered as a possible differential diagnosis.

References

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