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Case Report

Diffuse Infiltrative Gastrointestinal Lipomatosis in a Guinea Pig (*Cavia porcellus*)

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An intact adult male guinea pig (*Cavia porcellus*) went into cardiopulmonary arrest during a surgical procedure, and efforts at resuscitation were unsuccessful. Gross examination revealed a gastric rupture along the greater curvature of the stomach, which was associated with free blood and ingesta in the abdominal cavity, and a 2-cm nodular, partially circumferential, soft-to-firm mass within the pyloric region. Histologically, the pyloric mass was composed of sheets of infiltrative adipocytes expanding the muscular wall. Similar infiltrative sheets of adipocytes were present adjacent to the rupture site and within the small intestine, cecum, and colon. These findings are consistent with diffuse infiltrative lipomatosis, an exceedingly rare condition in human and veterinary species. This report is the first description of this rare disease in guinea pigs, and the concurrent involvement of both the stomach and intestines has not been reported in any veterinary species.

Gastrointestinal lipomatosis is a poorly understood, spontaneous disease in humans that is characterized by the presence of either multiple lipomas or multifocal infiltration of mature adipose tissue into the intestinal submucosal or subserosal layers, with disruption of the tunica muscularis.[3,7] The current case report describes diffuse gastrointestinal lipomatosis involving the stomach, small intestines, and colon that was associated with gastric rupture in a guinea pig. Infiltrative lipomatosis, the form found in the current case, is exceedingly rare in humans and veterinary species and, to our knowledge, has not previously been reported in laboratory animals. Furthermore, the observed involvement of the upper and lower digestive tract has not been documented in any veterinary species.

Case Report

A 13-mo-old male, pigmented, adenovirus-free guinea pig (*Cavia porcellus*) was a University of Michigan colony animal involved in a hearing study. The guinea pig was anesthetized by using intramuscular and subcutaneous injections of ketamine and xylazine and placed in ventral recumbency for an IACUC-approved surgical head-cap placement and cochlear implantation. Prior to surgery, the guinea pig was fed a commercial chow (LabDiet 5025 Guinea Pig Diet, LabDiets, St Louis, MO) and hay; the animal was last fed the evening before the day of surgery. The guinea pig was in good body condition, weighing 1302 g with a body condition score of 3.5 on a 5-point scale. During the surgical procedure, the guinea pig went into cardiopulmonary arrest, and resuscitation efforts were unsuccessful. Gross necropsy revealed free blood and ingesta within the abdominal cavity and an approximately 3.5-cm rupture along the greater curvature of the stomach, with jagged, reddish-brown friable edges (Figure 1). There was a focal, 2-cm, soft-to-firm, partially circumferential, nodular mass within the pyloric region (Figure 2 A) just proximal to the pyloric sphincter; the mass expanded the muscular wall without significant protrusion into the lumen (Figure 2 B). Histologically, the wall of the pyloric region was markedly thickened by infiltrative sheets and lobules of mature adipose tissue, extending transmurally from the serosal surface to the muscularis mucosa, dissecting between and separating myofiber bundles within the inner circular and outer longitudinal tunica muscularis (Figure 3 A). There was multifocal myofiber degeneration, characterized by shrinkage, fragmentation, and hypereosinophilia of myofibers and nuclear pyknosis (Figure 3 B), and multifocal foci of spindyloid cells with Anitschkow-type nuclei in areas of degeneration (Figure 3 C). These cells had large nuclei with condensation of chromatin into a central band spanning the long nuclear axis; Anitschkow-type cells are primarily associated with regenerative or inflammatory responses in cardiac muscle.[8] In addition, there was disruption and effacement of myenteric plexi within affected regions (Figure 3 D). Adjacent to the rupture site were similar infiltrative sheets of adipocytes multifocally breaching the serosal surface and extending through the subjacent inner and outer tunica muscularis into the submucosa (Figure 4 A). Within the intestinal tract, there were multifocal infiltrative nests of adipocytes within the ileum, centered on small arterioles within the tunica muscularis (Figure 4 B). Marked, locally extensive infiltration of sheets of adipocytes was present within the cecum and colon (Figure 4 C). In the colon, the adipocyte infiltration extended from the serosal surface, breaching the inner and outer tunica muscularis, and focally disrupted the muscularis mucosa, extending into the underlying lamina propria (Figure 4 D). No other significant histologic findings for this case were noted.

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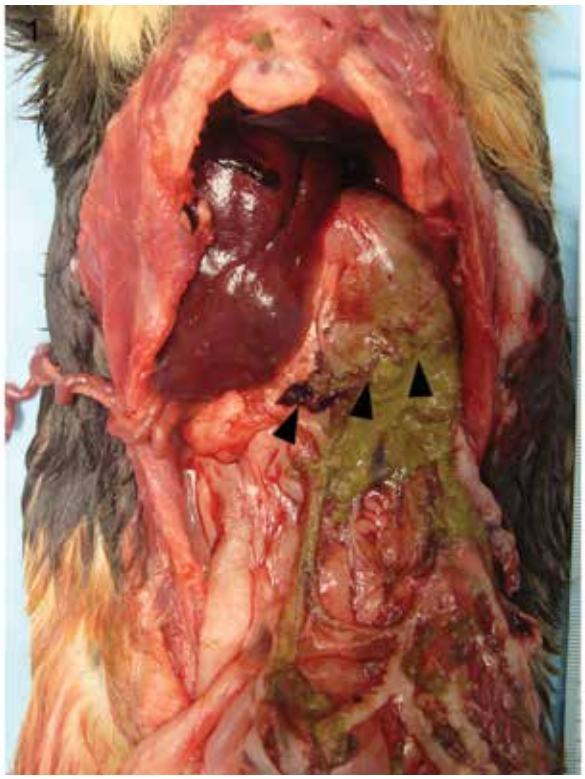

Figure 1. This photomicrograph of the abdominal cavity shows acute rupture along the greater curvature of stomach, with dark-red to brown irregular edges (arrowheads) and accompanying free blood clots and ingesta within the abdominal cavity.

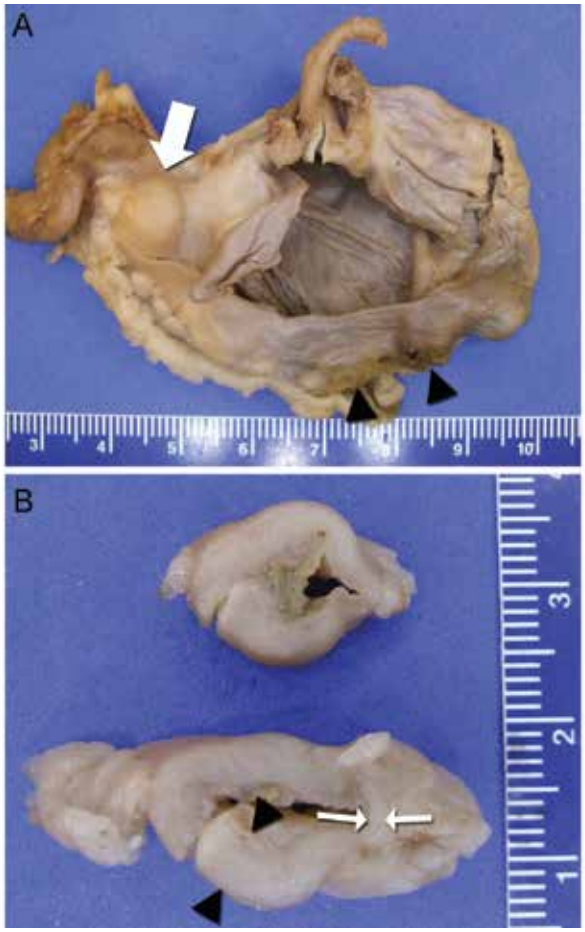

Figure 2. (A) This gross photomicrograph of the stomach after fixation shows the 3.5-cm rupture along greater curvature (black arrowheads) and a 2-cm nodular mass in the pyloric region (white arrow). (B) A cross-section of the pylorus adjacent to pyloric sphincter demonstrates marked, partially circumferential, thickening of the pyloric wall (black arrowheads) compared with adjacent normal wall thickness (white arrows).

Discussion

The histopathologic features of this case are consistent with diffuse infiltrative gastrointestinal lipomatosis. This lesion is very rare in humans and extremely rare in veterinary species.[2,4,7,10,11] The current case is the first report of this disease in the guinea pig and the first report of involvement of all segments of the gastrointestinal tract in any veterinary species. A disease syndrome termed 'bovine lipomatosis' has been described predominantly in Channel Island breeds of cattle but also in sheep, swine, and deer.[7] This form of the disease is generally associated with excessively fat cattle and is characterized by massive fat necrosis and inflammation within the peritoneal cavity and may be asymptomatic or fatal due to intestinal obstruction.[1,7] Although the disease names suggest a similar morphology, the gross and histologic lesions described in bovine lipomatosis differ greatly from those in the present case; consequently we feel that this guinea-pig case represents a separate disease entity that more closely resembles the diffuse infiltrative lipomatosis in humans. This guinea pig was not overconditioned and did not have excessive abdominal fat stores. Furthermore, there were no gross lesions of fat necrosis, and the histologic lesions were purely hyperplastic and infiltrative, rather than inflammatory and necrotic. To our knowledge, there is only one other case of diffuse infiltrative intestinal lipomatosis in the veterinary literature.[4] That lesion, which was documented in a horse, was characterized by numerous randomly scattered, multifocal to coalescing fatty masses along the serosal surface of the small and transverse colon, which histologically were proliferations of normal adipose tissue that invaded and effaced the longitudinal layer of the tunica muscularis.[4] The lesions in the horse did not involve the small intestine or stomach wall, as occurred in the present case.

In humans, intestinal lipomatosis is described as either the presence of multiple lipomas within the subserosal or submucosal layers of the gastrointestinal tract or as diffuse infiltration of these layers by adipose tissue.[3,10,11] Solitary lipomas occasionally are detected in the gastrointestinal tract in humans (4% to 8% of all gastrointestinal tumors),[5] but the incidence of lipomatosis is very rare. Furthermore, the diffuse infiltrative form is exceedingly rare, with fewer than a dozen case reports involving the intestinal tract[3,11] and only 2 reports that describe diffuse infiltration of the stomach wall.[5] To our knowledge, only 2 case reports in humans document simultaneous involvement of the stomach and intestine.[2,10] The etiopathogenesis of this disease

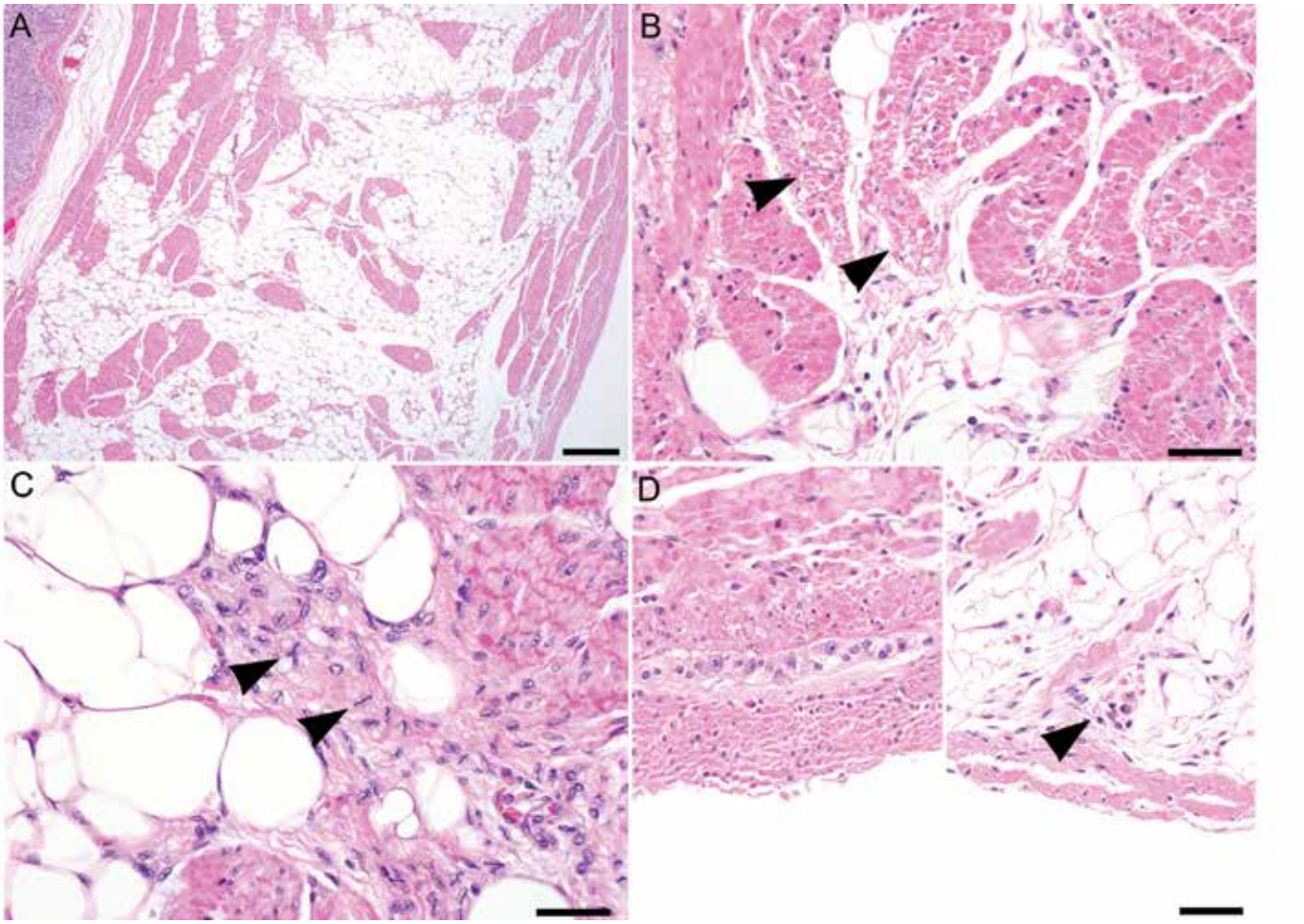

Figure 3. (A) There is marked thickening of pyloric wall, with infiltrative sheets and lobules of well-differentiated adipocytes causing separation, individualization, and loss of myofiber bundles (magnification, 4×; bar, 200 µm). (B) Multifocal myofiber degeneration (arrowheads) within the pyloric wall is characterized by nuclear pyknosis and myofiber shrinkage, fragmentation, and hypereosinophilia (magnification, 40×; bar, 25 µm). (C) Multifocal spindle cell proliferation is present, accompanied by several enlarged, hyperchromatic nuclei with centrally condensed bar-shaped chromatin (Anitschkow-type cells, arrowheads) (magnification, 40×; bar, 25 µm). (D) Normal myenteric plexus (left) compared with a disrupted and effaced myenteric plexus (right, arrowhead) in regions of adipose tissue infiltration (magnification, 40×; bar, 25 µm). Hematoxylin and eosin stain.

in humans is unknown, but some hypotheses include abnormalities in embryonic development, embryonic displacement of adipose tissue, hereditary disorders, disturbances of fat metabolism, and hamartomatous syndromes involving mutations of tumor suppressor genes such as *PTEN* and *NF1*.[6,12] Mutations of these tumor suppressor genes are associated with Proteus and Proteus-like syndromes characterized by limb asymmetry, cerebral malformations, vascular malformations, and overgrowth of multiple tissues including connective tissue, epidermal nevi, and lipomatosis.[6,9,12]

The exact cause of the gastric rupture observed in the guinea pig remains unclear. The animal had no prior health concerns and no known history of trauma that might have predisposed it to such a lesion. Furthermore, because this animal was asymptomatic, whether preventative measures, such as a low-fat diet, might have been effective is unknown. Few data regarding the pathophysiology of this disease and whether dietary factors play a role in the diffuse infiltrative form, as seen in humans, are available in the literature. It is clear that the integrity of the stomach wall, both at the rupture site and in the pylorus, was compromised due to extensive adipocyte infiltration in our guinea pig. Perhaps the fundus was at increased risk of perforation secondary to adipose infiltration than was the relatively thicker pylorus. The loss of myofibers and myenteric plexi in the pyloric region likely led to altered peristaltic function and decreased pyloric outflow, with a resultant delay in gastric emptying. Although not a reported feature of the current case, gastric dilatation (bloat) is a potential complication that might have occurred during anesthesia and thus if present, may have been a contributing factor in this animal's demise. However, more likely, any resuscitation efforts that increased intraabdominal pressure may have played a role in the development of rupture in an already compromised stomach wall. Whether the gastric rupture occurred as a primary inciting factor in cardiopulmonary collapse or was secondary to resuscitation efforts during an anesthetic arrest is unknown. In any case, increased gastric pressure coupled with loss of integrity of the stomach wall, altered peristaltic function, and decreased pyloric outflow due to diffuse infiltrative gastrointestinal lipomatosis may have contributed to the gastric rupture in this case.

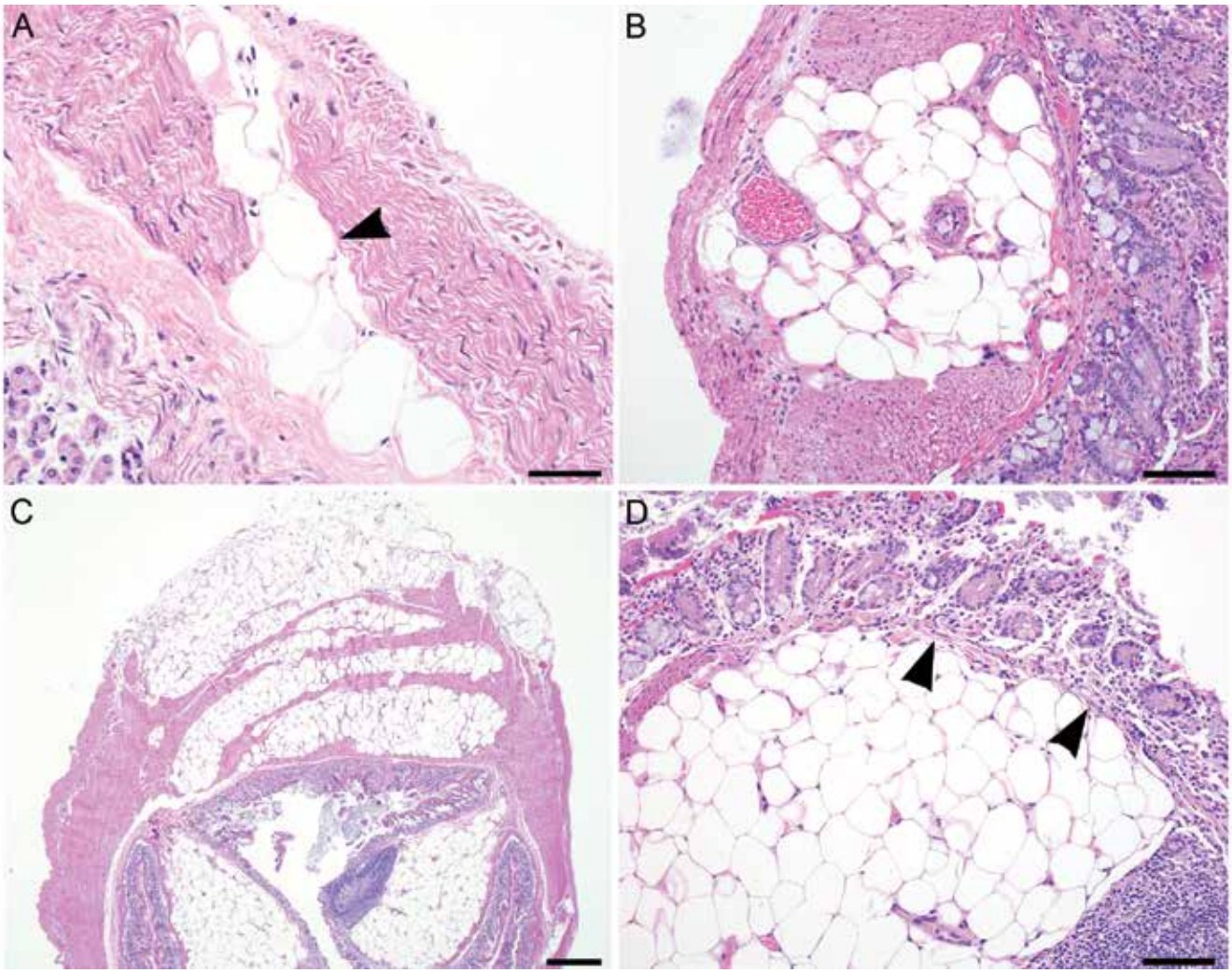

Figure 4. (A) A section adjacent to the rupture site shows focal infiltration of adipose tissue (arrowhead) from the serosal surface through the tunica muscularis and into the underling submucosa (magnification, 40×). (B) In sections of ileum, multifocal adipocyte infiltration is centered on small arterioles within the tunica muscularis (magnification, 20×; bar, 50 µm). (C) In sections of colon, there is locally extensive infiltration of sheets of adipocytes from the serosal surface through the tunica muscularis to the submucosa (magnification, 4×; bar, 200 µm). (D) Focal breach of the muscularis mucosa by infiltrating adipocytes into the underlying lamina propria of the colon (arrowheads; magnification, 20×; bar, 50 µm). Hematoxylin and eosin stain.

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