Gypsy's GI Nightmare

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Introduction

Intestinal adenocarcinomas are rare in dogs and represent 0.3% of canine malignancies. [4] The most common intestinal neoplasm in dogs is lymphoma, at approximately 6% of canine tumors, followed by adenocarcinoma and then leiomyosarcomas. [1,8] Clinical signs vary depending on tumor type and location. Some of the most common clinical signs can include varying degrees of anorexia, vomiting, gastrointestinal bleeding and diarrhea.[1,5] For adenocarcinomas, the treatment of choice tends to be surgical resection depending on location, and there is limited evidence to support chemotherapy in adding with survival time. [3,8]

History and Presentation:

This case involved an approximately 6-year-old female spayed Chesapeake Bay Retriever who presented to MSU-CVM Small Animal Emergency Services on 2/18/2020 for an approximately 1-2-month history of diarrhea and weight loss. The diarrhea did not have any mucous, and she was not exhibiting any tenesmus. Initially, the stool appeared normal with frank blood then progressed to diarrhea with melena. Two weeks prior to presentation, she began vomiting food and bile intermittently and did not appear to be associated with feedings. Her appetite decreased on 2/16. The degree of vomiting and diarrhea could not be quantified due to the amount of time the patient spent outdoors.

She was up to date on vaccinations and received Nexgard and Interceptor for flea/tick/heartworm prevention. Her referring veterinarian had attempted to treat the diarrhea in the past with metronidazole, sulfasalazine and Cerenia.

Upon initial presentation to MSU-CVM, she was anxious, alert, and responsive. She appeared to be 5-7% dehydrated with pink and tacky mucous membranes, a capillary refill time of less than 2 seconds, and a body condition score of 3/9. She had a pulse rate of 160bpm, was panting and had a temperature of 102.1F. On TFAST scan, B-lines and pleural effusion were visualized bilaterally. She had enlarged submandibular lymph nodes, enlarged inguinal lymph nodes, and melena. The remainder of her physical exam was within normal limits.

Diagnostics

For initial work-up, a fecal flotation was performed; no ova or coccidia were seen. A 4Dx snap test was performed which was also negative.

Her bloodwork showed a mild leukocytosis at 24.86 10^3/ µL (7.00-22.00). She had a moderate neutrophilia at 22871 /µL (3500-14200) which could be attributed to corticosteroid effects coupled with an inflammatory effect. She had a monocyte count of 0 /µL (3-10) which is non-diagnostic. She was hypoproteinemic at 5.7 g/dL (6.0-7.5), and her albumin was 2.0 g/dL (2.5-3.9). The hypoproteinemia and hypoalbuminemia could be due to gastrointestinal losses, decreased absorption, or decreased production from the liver. There was an elevated ALP at 333 U/L (11-140) which could be due to corticosteroid effects or cholestasis. The ALT was 299 U/L (10-90) which indicated direct hepatocellular damage. Her magnesium was at 1.6 mg/dL (1.7-2.4) which could be due to decreased absorption or individual variation. A coagulation panel was within normal limits. Following bloodwork, diagnostic imaging was performed.

Abdominal radiographs were performed to further evaluate the vomiting, diarrhea, and melena. There was a focal decrease in peritoneal serosal detail in the cranial abdomen which could be due to peritoneal effusion, organ crowding, or peritonitis. There were several round

structures in the pylorus and proximal descending duodenum with smooth, undulating margins. One of these structures was confluent with the pyloric margins, and the others were surrounded by gas. The largest measured approximately 3.3X2.5cm. These could be tumors of infectious or neoplastic etiologies, gastric polyps, and less likely foreign material or food. The descending duodenum was gas distended with undulating mucosal margins. Other segments of small intestine were filled with heterogenous gas and fluid opaque material. Other modalities that could have been implemented in this case were contrast upper gastrointestinal radiographic study or computed tomography. Contrast radiography could have helped to visualize any obstructed areas easier as well as helped to localize specific tumor locations.[8] While advancements in ultrasound have made this modality less necessary, it would have been helpful in cases like this where visualization can be impeded by the gas that was present in the pylorus and duodenum.

Abdominal ultrasound was performed and revealed an irregularly shaped, ill-defined mass measuring 2.32cm within the pylorus and descending duodenum. The wall of the duodenum was diffusely thickened measuring 0.64cm (<0.53cm)[7], with a loss of normal wall layering. This could be due to neoplasia or another infiltrative disease like pythiosis. One study found that 99% of dogs with intestinal tumors had loss of normal wall layering when differentiating between intestinal neoplasm vs enteritis. [6,8] This study found that intestinal tumors commonly have thickened walls and loss of layering.[6] There were multiple enlarged lymph nodes present throughout the abdomen with the largest measuring 1.56cm in diameter, which could be due to metastatic neoplasia or reactive lymphadenopathy. Normal lymph node size can vary depending on the animal.[7] In the aforementioned study that used abdominal ultrasound to differentiate between enteritis vs neoplasia, lymph node thickness in neoplasia ranged from 0.3-9.0cm, while in enteritis it ranged from 0.6-2.6cm.[6] Because pythiosis can mimic neoplasia on

abdominal ultrasound and was a differential, Pythium titers were submitted. At 1:2000 and 1:4000 dilutions, results were 2% and 1% respectively. Anything less than 40% of the positive control values are considered negative at all dilutions, making neoplasia the top differential.

Gastric aspirates were obtained during ultrasound, but the slides were poorly cellular and inconclusive. A biopsy was recommended for better evaluation.

Because the TFAST scan revealed B-lines and pleural effusion, thoracic radiographs were obtained. There was rounding of the lung margins, widening of the interlobar fissures, and border effacement of the cardiac silhouette and diaphragm, all consistent with pleural effusion. A thoracocentesis was performed to obtain fluid for analysis, which was consistent with a possible epithelial neoplasm. There was a mild diffuse unstructured interstitial pulmonary pattern that appeared worse in the right caudal lung fields, which was likely due to the suspected neoplasia and edema but could result from atelectasis or infectious/inflammatory etiologies. There was a diffuse bronchial pulmonary pattern which could be bronchitis due to infectious/inflammatory etiologies or age related. A bony callus was present along the middle aspect of the 9th rib.

On endoscopy, there was a multilobulated, erythemic mass within the pylorus. The endoscope could not be passed beyond the mass to evaluate the duodenum. Biopsy of the mass was performed by a snare, which was consistent with adenomatous polyps. One study showed that endoscopic biopsies do not commonly match the diagnosis from full thickness surgical biopsies due to the superficial samples typically obtained via endoscope. [3]

Other diagnostic that were considered but not pursued in this case were computerized tomography (CT) scan and exploratory laparotomy. With exploratory laparotomy, the observer

achieves direct visualization of the entirety of the abdominal viscera and contents. This gives the opportunity to obtain full thickness biopsies and can allow for resection of some tumors.

Necropsy Findings

In the abdominal cavity, there was ~100ml of yellow to tan, thin, translucent fluid. The omentum had widely disseminated, 1-2mm, firm, white nodules. These nodules were present throughout the abdomen. On the left lobe of the pancreas, there was a multinodular mass that was irregularly marginated, firm, and pink to tan. The liver was diffusely pale and enlarged with rounded margins. In the distal portion of the pylorus were two nodules measuring 1x1.5x2cm and 2.5x2.5x1cm that were white, firm, and irregularly marginated. Between these two nodules there was a chronic ulcer, measuring 1.5x1cm with thickened, pale tan margins. Affecting ~15cm of the proximal duodenum there was circumferential, irregular, multinodular thickening of the duodenal wall. The thickening appeared to be mostly localized to the mucosa. The small intestines were full of yellow to black ingesta. There was a 2.5x2.5x1cm irregularly marginated, white, firm mass in the jejunum.

In the thoracic cavity, there was ~500ml of yellow to red fluid. The white, circular, well-demarcated, firm nodules that were in the abdomen were also present throughout the thoracic cavity. The lungs were poorly collapsed and mottled dark red with multifocal pale red to tan foci on the pleural surface.

On histopathology, there was expansion of the duodenal mucosa by neoplastic epithelial cells forming papilliferous projections into the lumen and invading the underlying submucosa. There was moderate anisocytosis and marked anisokaryosis with 41 mitotic figures in ten 400x fields. As mentioned earlier, duodenal adenocarcinomas can be further classified as acinar,

papillary, solid, mucinous, or carcinoid. In this case, her tumors show characteristics of both acinar and papillary.[5] Similar neoplastic cells were found within lymphatics, lymph nodes and invading into the pancreas.

In the lungs and on the pleural surface, there were neoplastic cells similar to those found in the duodenum. Frequently entrapped within the neoplastic cells of the pleura and mediastinum were ovoid or irregular trematode eggs with a golden-brown capsule consistent with *Paragonimus kellicotti* or *Heterobilharzia americana*.

Pathophysiology

This patient was diagnosed with duodenal adenocarcinoma with carcinomatosis. Intestinal tumors are rare in dogs and can arise from all tumor types. It is important to note that most small intestinal tumors in dogs are malignant.[8] Clinical signs are dependent on location in the gastrointestinal tract. With small intestinal neoplasms, vomiting, anorexia, diarrhea, weight loss and melena are commonly seen. With large intestine/rectal neoplasms, clinical signs are similar but can include hematochezia and tenesmus.[5] A common finding with intestinal adenocarcinomas is anemia of chronic disease, but that was not present in this case.[4] Intestinal neoplasia can occur anywhere in the gastrointestinal tract, and in the present case arose from the duodenal mucosal epithelium consistent with an adenocarcinoma. This tumor then metastasized through the lymphatics to other organs. Carcinomatosis was seen in the abdomen and thorax along all serosal layers and penetrating the parenchyma of other tissues. Carcinomatosis indicates disseminated metastases via tumor seeding throughout the peritoneal and, in this case, pleural cavities. The presence of carcinomatosis does not mean that the animal needs to be euthanized but does tend to carry a poor prognosis. [8]

Intestinal adenocarcinomas can be subdivided into categories based on their histopathologic classifications including acinar, papillary, solid, mucinous, or carcinoid. [5] The most common clinical signs for duodenal adenocarcinomas include anorexia, post-prandial vomiting and depression, weight loss, melena, and diarrhea.[1,5] One study found that 40% of dogs have metastasis at the time of diagnosis. [4] This is most likely due to diagnosis occurring late in the disease process. Most studies find that males and females share an equal incidence of intestinal adenocarcinoma, but some studies show males are more predisposed. [8] Common sites of metastases for intestinal tumors include the mesenteric lymph nodes, liver, mesentery, omentum, spleen, kidney, bone, peritoneum/carcinomatosis, and lung.[8]

The median survival time (MST) in dogs with intestinal adenocarcinomas differed depending on whether metastases were located and found histologically. One study suggests that MST is 10 months with a one-year survival rate at 40.9% on average. For dogs with histologically documented metastases, the MST was 3 months with a one-year survival rate at 20%. If no metastases were detected, the MST was 15 months with a one-year survival rate at 66.7%.[1] Another study found that gender affected MST in dogs with intestinal adenocarcinoma, stating females lived a median of 28 days while males lived a median of 272 days. [4]

Treatment

The treatment of choice for intestinal neoplasia, apart from lymphoma, is surgical resection. It should be noted that mortality can reach 30-50% perioperatively as a result of sepsis, peritonitis, or euthanasia due to the tumor being nonresectable.[8] There is limited evidence to the use of adjunctive chemotherapy in the case of intestinal tumors in the dog. The systemic chemotherapeutic agents include doxorubicin and carboplatin regimens; however, intracavitary chemotherapy (carboplatin and mitoxantrone) has been shown to be well tolerated and to

improve symptoms that occur due to effusive carcinomatosis. [3] Radiation therapy is not commonly used due to the fears of causing toxicity to the surrounding abdominal viscera.[3]

Due to the severity of tumor involvement, a pylorectomy with gastrojejunostomy (Bilroth II) would have been necessary. This involves resection of the pylorus and duodenum with re-routing of the bile duct. This is because the common bile duct inserts into the duodenum at the duodenal papilla. These dogs tend to have complications with bacterial overgrowth as jejunal bacteria make its way up to the gall bladder. Prognosis for this procedure is guarded to poor.[3]

In this case, the patient was discharged with a presumptive diagnosis of gastric adenocarcinoma. She was sent home on Cerenia 2.5mg/kg every 24 hours for nausea and vomiting, Metronidazole 10.5mg/kg every 12 hours, Omeprazole 0.8mg/kg every 12 hours for gastrointestinal ulcer protection and treatment, Sucralfate 41.8mg/kg every 8 hours as a gastrointestinal mucosal protectant, and Fenbendazole 50mg/kg once. She presented again to MSU-CVM Small Animal Internal Medicine Department two days after discharge with worsening clinical signs. Her owners elected euthanasia, and she was sent to MSU-CVM Pathology Department for necropsy.

Conclusion

Lymphoma is the most common intestinal neoplasia found in the dog, followed by adenocarcinoma.[8] Clinical signs of intestinal adenocarcinoma are largely dependent on location in the gastrointestinal tract, but mostly include vomiting, lethargy, weight loss, melena, anorexia, hematochezia, and tenesmus.[8] Diagnostic work-up should include abdominal/thoracic radiographs and abdominal ultrasound, or other modalities of advanced imaging depending on the case. Definitive diagnosis is achieved through endoscopic or surgical biopsy, with the

understanding endoscopic biopsies may be unrewarding due to the sample size. Treatment for these patients generally involves surgical resection with limited evidence supporting the use of adjunctive chemotherapy.[3] MST is ~10 months but was most likely lower in this case due to the severity of disease.[1]

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