The Luck of the Draw: A Case of Recurrent Colic

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Introduction

Colic is the term used to describe acute abdominal pain in the horse, and it is most commonly associated with gastrointestinal disease[6]. Recurrent colic can be defined as repeated bouts of colic, with a time period of remission of clinical signs between episodes[13]. Clinical judgment must be used to determine whether the time period of remission between episodes allows for classification of recurrent colic, but in general, recurrent colic can be described as at least two episodes of colic with a period of time of at least 48 hours between episodes[2,11]. These colic episodes often last less than 24 hours at a time and can prove difficult to diagnose, particularly if the patient presents without active signs of colic. Recurrent colic can be due to extra-intestinal causes such as urogenital, hepatic, splenic, and pancreatic disorders, but it is more commonly gastrointestinal in origin[13]. Potential gastrointestinal causes for recurrent colic include but are not limited to gastric pain due to gastric ulcers; small intestinal stenosis due to wall thickening, partial obstruction (foreign body, enterolithiasis, etc), or incomplete displacement (diaphragmatic hernia, intussusception, etc); motility disorders due to feeding management or dental care, stress, or intestinal parasites; and finally neoplasia[13].

Neoplasia of the gastrointestinal tract is quite rare in horses[14], and accounts for less than 10% of recurrent or chronic colic cases diagnosed by a veterinarian, according to two studies by Mair and Hillyer[6,8]. Alimentary lymphoma is the most common intestinal neoplasia in the horse[15]. In a study performed at the University of California, lymphoma was the most common intestinal neoplasm, followed by adenocarcinoma and smooth muscle tumors such as leiomyomas and leiomyosarcomas[14]. The small intestine was most frequently affected compared to the rest of the gastrointestinal tract. The median time from onset of clinical signs to death or euthanasia was less than two months, illustrating the grave long-term prognosis of horses with

intestinal neoplasia.

History and Presentation

A 5-year-old Quarter Horse mare presented to Mississippi State University College of Veterinary Medicine (MSU-CVM) on February 18, 2016, with a one month history of mild, recurrent colic. Recurrence rate was approximately once weekly during the month prior to presentation, with three separate other occurrences within the last seven months. The patient was used for Western pleasure and trail riding and had been stabled at her trainer's barn in Pensacola, Florida, for the past 10 months. The mare was fed three pounds of Nutrina healthy choice twice daily, shod every six weeks, and had her teeth floated once a year in March. She was stalled 80% of the day and turned out to pasture 20% of the day. The pasture's soil was a combination of clay and sand with grass for grazing. The patient's colic episodes first coincided with a change in feed from peanut hay to Bahia hay and a new stall location. Clinical signs at that time included pawing, striking, and inappetence. Episodes of colic lasted no more than 24 hours and were treated by the trainer with single doses of flunixin meglumine (1.1 mg/kg) intravenously for each episode. Her clinical signs became more frequent prior to presentation at MSU-CVM, and her last dose of flunixin meglumine was at 3:00 AM the morning of presentation. The owner expressed concerns of an enterolith, due to the fact that the mare's half sibling, who lived in the same area, died the previous year after being diagnosed with enterolithiasis.

Upon presentation, the mare was quiet, but alert and responsive. She weighed 1,048 pounds and was in ideal body condition with a body condition score of 5/9. Her vital parameters were within normal limits (temperature 99.9˚F, heart rate 36 beats per minute, respiratory rate 20 breaths per minute). Her mucous membranes were tacky but pink with a capillary refill time of 3 seconds, and there was a moderate skin tent present. There were decreased gut sounds in all four

quadrants of the abdomen, and there was dried blood in the left nostril, indicative of previous nasogastric intubation by her trainer. The rest of her physical exam was within normal limits.

Diagnostic Approach

Rectal palpation was performed and was within normal limits. Gastroscopy revealed a large obstructive food bolus in the stomach. A nasogastric tube was placed, and the stomach was copiously lavaged and refluxed with 60 liters of water to resolve the obstruction. The nasogastric tube was taped in place to facilitate further fluid administration. Abdominal ultrasound revealed no abnormal findings. Complete blood count revealed a mild, mature neutrophilia of 6,983.6/uL (2,500-6,000/uL). Serum chemistry revealed a mild hyperglycemia of 187 mg/dl (60-122 mg/dl), moderate azotemia with a BUN of 35 mg/dl (10-24 mg/dl) and creatinine of 2.72 mg/dl (1.20-1.90 mg/dl), mild hyperphosphatemia of 4.4 mg/dl (2.4-4.0 mg/dl), mild hypercholesterolemia of 129 mg/dl (78-120 mg/dl), and an moderately increased CK of 716 U/L (57-283 U/L).

The patient was treated overnight (every 2 hours) with 4L of alternating water and electrolyte solution via nasogastric tube. Lactated ringers solution spiked with potassium chloride and calcium gluconate was administered intravenously at a maintenance rate overnight to correct dehydration. A net total of 5 liters were refluxed between 7:00pm and 10:00pm, and her nasogastric tube was removed at 10:00pm. Gastroprotectants were administered orally every eight hours (7 mg/kg ranitidine and 25 mg/kg sucralfate).

The following morning, the mare was bright, alert, and responsive. Repeat serum chemistry was largely within normal limits, with the exception of a still elevated CK of 445 U/L (57-283 U/L). Her azotemia had resolved with fluid administration, indicating a pre-renal azotemia from the previous day. Repeat gastroscopy revealed resolution of the obstructive food bolus. The glandular mucosa was hyperemic but there was no evidence of gastric ulcers. There

were two bot fly larvae attached at the margo plicatus. The pyloric sphincter had two distinct linear areas of hyperemia. Because clinical signs had not completely resolved, and the owner expressed concerns about possible enteroliths, abdominal radiographs were performed. Abdominal radiographs revealed a round, soft tissue opaque structure in the caudal abdomen, with consideration given to a foreign body or enterolith. Smaller mineral opacities were also visualized in the caudal abdomen, which appeared to be sand within the large colon. An exploratory laparotomy was performed to remove what appeared to be a foreign body on radiographs.

A ventral midline celiotomy was performed under general anesthesia. There were approximately 5.5 meters of markedly dilated jejunum to proximal ileum, about three times normal. The serosal surface of the jejunum had multifocal, round, firm, white, 2-5 millimeters nodules forming linear patterns along the serosal vessels in an area approximately 10 centimeters long. The intestinal wall was firm and markedly thickened upon palpation. Two full thickness biopsies of the jejunum and fine needle aspirates of the nodules were taken. Cytologic evaluation of the nodules revealed a proliferation of spindle cells, consistent with neoplasia. Surgical resection of the affected tissue would have required a jejunocecostomy to remove all affected tissue. After discussing the poor prognosis, the owner elected humane euthanasia while the mare was still anesthetized.

Necropsy

Gross findings were consistent with what was visualized at surgery. There were approximately 5.5 meters of markedly dilated jejunum to proximal ileum, measuring 15 centimeters in width, with moderate thickening of the wall that was 1.5 centimeters in width. The mucosa was mildly thickened and the tunica muscularis was markedly thickened. The mucosal

surface was erythematous and irregular in appearance. There were two locally extensive areas of the serosal surface that contained 2mm wide, firm, white nodules. One of these locations is where biopsies were taken and had marked thickening of the intestinal wall with a decreased lumen diameter.

Histopathology

Within the affected small intestine, focused primarily at the locations with decreased lumen diameter (not dilated), were multiple well demarcated masses that extend transmural from the submucosa, through the muscular layers, to the serosa. The masses were composed of interlacing fascicles of elongate spindle cells. Neoplastic spindle cells had elongate nuclei, finely stippled chromatin, and scant to moderate cytoplasm. There were rare mitotic figures. Additionally, there were scattered nodules localized either to the submucosa, myenteric plexus, or subserosa. The subserosal nodules corresponded with what was seen grossly at surgery.

The neoplastic cells stained immunopositive for S-100, indicating Schwann cell origin[3]. In some nodules, approximately 50% of the cells were immunopositive, while in others almost 100% of the spindle cells were immunopositive. In nodules with a lower percentage of S-100 staining, Masson's trichrome stain demonstrated collagen separating spindle cells within the neoplastic nodules, consistent with neurofibroma. Neurofibromas are comprised of Schwann cells, perineural cells, and fibroblasts. Interestingly, in some nodules, a subsest of the neoplastic cells were immunopositive for desmin and smooth muscle actin, indicating that the neoplastic cells have myogenic differentiation, which is rather unexpected.

In addition to intestinal wall expansion by neoplastic nodules, there was circumferential expansion of the muscular layers due to muscular hypertrophy. This change was marked in areas with luminal stenosis and not as severe in the dilated segments. An interesting histologic finding

throughout the affected small intestine was expansion of the myenteric plexus characterized by increased nerve fibers and large ganglion cells, consistent with hyperplasia of the myenteric plexus.

Pathophysiology

Peripheral nerve sheath tumors (PNST) are neoplasms that arise from the connective tissues surrounding peripheral nerves, including Schwann cells, fibroblasts, and perineural cells[5]. Schwannomas comprise entirely of Schwann cells, whereas neurofibromas comprise of Schwann cells, fibroblasts, and other perineural cells[16]. Ganglioneuromas are related, but arise from ganglion cells and are composed of nerve processes, neurons, and Schwann cells[4]. Determining the cell of origin of a PNST is often difficult, as there are not reliable and agreed upon immuno-histochemical markers for these tumors, especially in veterinary medicine[16]. Neurofibromas are more commonly found in the subcutis in veterinary medicine, but there have been reports of intestinal neurofibromatosis with diffuse ganglioneuromatosis diagnosed in two young canines in the colon and rectum[12].

The term gastrointestinal neurofibromatosis has been applied to a group of human genetic conditions that result in neurofibromas or ganglioneuromas, the most common genetic condition being Neurofibromatosis-1 (NF-1). Intestinal tumors associated with NF-1 are similar to those in this report. Patients with NF-1 multifocal neoplastic nodules composed of neurofibromas or ganglioneuromas within the intestinal wall often arise from the myenteric plexus. Interestingly, these tumors arise from multiple sites simultaneously in a segmental or regional area of intestine. Hyperplasia of the submucosal or myenteric plexus is often reported in NF-1[17]. In our case, the mare had multiple small intestinal neurofibromas with hyperplasia of the myenteric plexus and muscular hypertrophy.

The stenosis caused by the neoplastic masses and muscular hypertrophy resulted in a partial obstruction, similar to a foreign body or enterolith, as was initially suspected. The marked dilation of a large segment of small intestine contributed to altered motility and colic signs[1]. The dilation and muscular hypertrophy are thought to be secondary to the myenteric hyperplasia, thereby altering innervation and motility. These factors all contributed to the colic signs exhibited by this mare.

Treatment and Management

Surgical resection is the best therapy for a benign peripheral nerve sheath tumor, whether localized or multi-centric, so long as all the neoplastic tissue is resectable. In a case report from 1996, a 6-year-old gelding survived at least one year after surgical resection of three meters of distal jejunum and ileum, with multiple 10 millimeter nodules (diagnosed as neurofibromas and Schwannomas) extending over a length of 20 centimeters[7]. This case had muscular hypertrophy with subsequent cranial dilation, similar to the case described herein[7]. There was no further follow-up after twelve months. Similarly, an approximately 24 centimeter in length colonic neurofibroma was successfully resected in a 16-year-old mare with an acute episode of colic[9]. The mare remained in hospital for seventeen days post-operatively, but was in excellent condition thirteen months later[9].

Case Outcome and Conclusion

Humane euthanasia was elected by the owner due to the poor prognosis of intestinal neoplasia. Although there are reports of successful resection of peripheral nerve sheath tumors, we did not have that final diagnosis at the time of surgery, and were concerned it was a malignant neoplasm with metastasis[7,9]. It was more likely for the mare to have a malignant neoplasm such as lymphoma or adenocarcinoma than a rarity such as neurofibromatosis[14].

Furthermore, at the time of surgery, it was evident that approximately 5.5 meters of small intestine were involved, and would require a jejunocecostomy for complete resection. Post-operative success in horses with jejunocecal anastomoses varies from 37-83% of horses surviving to discharge, with an increased likelihood of recurrent colic within two years[17]. Managing post-operative ileus in this case with such a length of intestine resected would have proved a challenge, and could ultimately have resulted in the need for euthanasia as well. No genetic testing was performed in this case, but it would be interesting to know if a genetic defect, similar to several human conditions, was the cause.

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