Clinical Case
Presentation and Diagnosis

A 10-week-old, 110-kg quarter horse colt was referred to the North Carolina State University Veterinary Teaching Hospital for evaluation of an acute, 4-hour episode of colic. The colic was characterized by rolling and other signs of moderate to severe pain that were unresponsive to flunixin meglumine (1.1 mg/kg IV) administered by the referring veterinarian. The foal was dewormed once with fenbendazole approximately 1 week before presentation and was housed in a grass pasture with its dam. All other mares and foals on the same pasture were healthy. No other animals on the farm were ill.

The foal was quiet and did not show signs of abdominal pain on presentation. The foal's heart rate, respiratory rate, and temperature were within normal limits. The frequency and amplitude of borborygmi were judged to be less than normal. No nasogastric reflux was obtained. Ultrasonographic examination of the abdomen revealed several loops of mildly distended small intestine that appeared hypomotile. The intestinal wall thickness and structure appeared normal. Peritoneal fluid obtained by abdominocentesis had an elevated protein concentration (3.1 g/dl [normal, less than 2.0 g/dl]). The white blood cell count and cytology were normal. Mild leukocytosis (13,100 cells/µl [reference range, 6100 to 12,100/µl]), erythrocytosis (10.84 x 10⁶ cells/µl [reference range, 5.90 to 9.80 x 10⁶/µl]), and thrombocytosis (280,000 cells/µl [reference range, 94,000 to 232,000/µl]) were detected at presentation. The neutrophil and eosinophil counts were not determined.

Biochemical analysis revealed hypoalbuminemia (2.3 g/dl [reference range, 3.0 to 4.8 g/dl]), hyperglycemia (144 mg/dl [reference range, 65 to 110 mg/dl]), and mild hypocalcemia (11.1 mg/dl [reference range, 11.5 to 14.2 mg/dl]). The calcium concentration was normal when corrected for hypoalbuminemia. Venous blood gas analysis was normal, including ionized calcium concentrations.

A McMaster's quantitative fecal egg test did not detect any parasite eggs.

The foal was placed into a stall and monitored for pain. Approximately 2 hours after admission, the colt became uncomfortable and depressed. A second ultrasonographic examination of the abdomen revealed a greater proportion of distended small intestine than was detected on initial examination. The degree of distension was also judged to be greater than that on initial examination. Motility still appeared to be less than normal. The decision was made to perform an exploratory celiotomy based on the recurrent pain and ultrasonographic evidence suggestive of progressive small intestinal distension. Ampicillin sodium (22 mg/kg IV) and amikacin (22 mg/kg IV) were administered before surgery. A ventral midline celiotomy was performed. Examination of the small intestine revealed a 2-cm (circumference), nodular lesion in the midjejunum causing a partial stricture with proximal distension of the small intestine. A wedge resection of the lesion was performed, and the resected tissue was submitted for histopathologic examination. The remaining gastrointestinal (GI) tract was examined, with no abnormalities identified. The abdomen was closed, and recovery from anesthesia was uneventful.

Histopathologic examination of the resected tissue revealed marked eosinophilic infiltration of the mucosa, submucosa, and tunica muscularis, with scattered lymphocytes and plasma cells (Figure 1). There were multifocal granulomas within the submucosa and tunica muscularis composed of a central core of eosinophilic debris surrounded by epithelioid macrophages and two to five layers of fibrous connective tissue, consistent with a diagnosis of focal, idiopathic eosinophilic enteritis.

IDIOPATHIC EOSINOPHILIC ENTERITIS IN A 10-WEEK-OLD COLT

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circumferential, idiopathic eosinophilic enteritis.¹⁻³

Treatment
Postoperative treatment consisted of ampicillin sodium (22 mg/kg IV q6h for 14 days), amikacin (22 mg/kg/day IV for 14 days), flunixin meglumine (1.1 mg/kg IV q12h for 4 days), cimetidine (6.6 mg/kg IV q8h for 3 days), and omeprazole (4 mg/kg/day PO for 35 days). One liter of J-5 plasma was administered after the foal recovered from anesthesia. Plasmalyte M® (Baxter Healthcare Co, Deerfield, IL) solution supplemented with 5% glucose was administered for 10 days (2.2 ml/kg/h). Lidocaine was administered as a constant infusion (1.3 mg/kg loading dose, then 0.05 mg/kg/min IV in 0.9% saline solution) for 48 hours after surgery. Starting the day after surgery, the foal was allowed to nurse from the mare for restricted periods of time. Several episodes of moderate abdominal pain during the first 48 hours after surgery were controlled with butorphanol tartrate (0.1 mg/kg IM as needed). The day after surgery, the colt became pyretic (39.7°C) and was intermittently febrile for 8 days. Diarrhea began 4 days after surgery. A complete blood cell count performed at the onset of the fever revealed neutropenia (468 cells/µl [reference range, 3400 to 8500 cells/µl]) with a left shift (396 band cells/µl [normal, 0 cells/µl]). Polymyxin B (2200 IU/kg IV q12h) administration was begun when neutropenia was detected and was discontinued 5 days later when neutropenia resolved. Metronidazole (22 mg/kg PO q8h for 10 days) administration and daily fecal cultures for Salmonella were initiated at the onset of diarrhea. Fecal culture was positive for Salmonella 6 days after diarrhea began. The diarrhea resolved after 5 days.

The foal became lethargic 2 days after antibiotic treatment was discontinued. Complete blood cell count revealed neutrophilia (14,470 cells/µl [reference range, 3400 to 8500 cells/µl]) and hyperfibrinogenemia (500 mg/dl [reference range, 100 to 400 mg/dl]). Abdominocentesis was attempted, but no peritoneal fluid was obtained. Ultrasonographic examination was not possible because the foal was in isolation. Chloramphenicol administration (50 mg/kg PO q6h) was begun. The foal was bright and alert 24 hours after the initiation of chloramphenicol treatment. The neutrophil count decreased but remained elevated (10,400 cells/µl) and the hyperfibrinogenemia had resolved 9 days after chloramphenicol treatment was begun. The hypalbuminemia persisted for the entire hospitalization period. The foal was discharged with instructions to continue chloramphenicol and omeprazole for 7 days and to de-worm the foal with ivermectin (0.2 mg/kg PO) within 1 week after discharge. The foal was doing well 3 months after discharge. It had no episodes of colic or diarrhea following discharge, and its growth rate was comparable to that of other foals its age on the farm.

Discussion
Eosinophilic enteritis causes weight loss, chronic intermittent colic, and diarrhea. Investigation of eosinophilic infiltrative diseases divides them into two distinct syndromes: multisystemic eosinophilic epitheliotropic disease and idiopathic eosinophilic enteritis.¹

Multisystemic Eosinophilic Epitheliotropic Disease
Multisystemic eosinophilic epitheliotropic disease affects horses older than 1 and younger than 4 years of age.¹⁻³ Clinical signs include moderate to severe weight loss, recurrent colic, dermatitis, and, occasionally, diarrhea. The disease is characterized pathologically by eosinophilic inflammation of multiple organs and tissues, including the skin (lesions on the face, limbs, and ventral portion of the abdomen), liver, mesenteric lymph nodes, and GI tract. The distribution of affected intestine may be either segmental or diffuse. Eosinophilic granulomas associated with vasculitis and fibrinoid necrosis of intramural vessels are present in an affected segment of large intestine, small intestine, or rectum. Eosinophilic granulomas may also be seen in liver, lymph nodes, or skin. This disease usually does not respond to antibiotics, anthelmintics, or corticosteroids. Its etiology has not been determined.

Idiopathic Eosinophilic Enteritis
Idiopathic eosinophilic enteritis involves the GI tract and possibly the mesenteric lymph nodes. Idiopathic eosinophilic enteritis is most commonly reported in horses older than 1 and younger than 4 years of age.¹⁻³ Histopathologic lesions consist of eosinophilic infiltration of all layers of the affected intestine, including the tunica muscularis, with circumferential fibrosis.¹⁻³ The fibrosis is manifested grossly by prominent circumferential bands. Chronic idiopathic eosinophilic enteritis is characterized by intermittent or chronic diarrhea and, occasionally, weight loss. The disease is characterized by eosinophilic infiltrate of the lamina propria, muscularis mucosa, and submucosa of the affected segment of the bowel. Eosinophils are present in the lamina propria and occasionally in the submucosa. The affected segment of intestine may be segmental or diffuse. The disease is characterized by intermittent or chronic diarrhea and, occasionally, weight loss. The disease is characterized by eosinophilic infiltrate of the lamina propria, muscularis mucosa, and submucosa of the affected segment of the bowel. Eosinophils are present in the lamina propria and occasionally in the submucosa. The affected segment of intestine may be segmental or diffuse.

Figure 1—Microscopic appearance of tissue obtained from a nodular, circumferential lesion resected from the midjejunum of a foal with acute signs of colic. Note the intense eosinophilic inflammation of the tunica submucosa adjacent to a lymphoid nodule (A) and the eosinophilic inflammation interspersed between smooth muscle cells of the tunica muscularis (B; hematoxylin & eosin, original magnification ×200).
enteritis is characterized clinically by intermittent colic, weight loss, and hypoproteinemiamia. Horses may also be presented with acute signs of moderate to severe colic without weight loss. Lesions associated with idiopathic eosinophilic enteritis can be singular or multiple and found in the small intestine, large intestine, or both. The lesions are usually discrete, but there has been one report of diffuse eosinophilic infiltration restricted to the small and large intestines that caused recurrent large colon impactions in a mare. Idiopathic eosinophilic enteritis is often diagnosed via exploratory celiotomy performed because of unresponsive, acute colic or chronic, recurrent colic. Treatment for idiopathic eosinophilic enteritis has included surgical resection of affected portions of the intestine followed by corticosteroid administration. The prognosis following surgical resection of the affected segment of intestine is favorable. Surgical resection without corticosteroid treatment was successful in the case reported here. Corticosteroid administration alone may also be effective if resection is not an option and the colic episodes can be controlled pharmacologically. Treatment with corticosteroids was not deemed wise in this foal due to the episode of salmonellosis following surgery and the good prognosis associated with surgical resection of the affected intestine.

The case reported here is remarkable because of the horse’s age. Neither the acute nor chronic form of idiopathic eosinophilic enteritis has been described in a horse younger than 1 year of age. The clinical and histopathologic features of the case reported here are most consistent with acute idiopathic eosinophilic enteritis. Eosinophilic inflammatory diseases are thought to be hypersensitivity reactions to persistent antigenic stimulation (e.g., food allergy, parasitism). The causative antigen source is rarely found in equine eosinophilic enteritis cases. Encapsulated parasites were observed in inflamed loci associated with eosinophilic enteritis in one report. While a parasitic cause could not be ruled out in this case, there was no evidence of parasitic infection. No parasites, foreign body, or other apparent antigenic stimulus was found on histopathologic examination.

### References


### CASE NOTES AND COMMENTARY

**IDIOPATHIC EOSINOPHILIC ENTERITIS: ETIOLOGY AND PATHOPHYSIOLOGY**

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Numerous types of lesions that fall within the realm of inflammatory bowel disease (IBD) occur spontaneously in horses. Clinical manifestations of such lesions, whether acute or chronic, have rarely been seen in foals younger than 6 months of age. More often than not, horses presented with clinical signs consistent with well-established IBD (progressive weight loss and hypoproteinemia) are older than 1 year of age. Thus the clinical presentation in this report was unusual not only because of the colt’s young age but also because the colt had acute colic due to physical obstruction of the jejunal lumen by a very focal lesion. It is interesting to note, however, that IBD lesions that have caused focal intestinal obstruction in horses or humans have often been eosinophilic and granulomatous in nature. This information makes me wonder whether the lesion in this case might represent an earlier manifestation of the far more extensive lesions that normally cause the clinical signs associated with IBD or whether this focal lesion would have remained clinically inapparent had it not obstructed the intestine. Clearly, the factors that govern whether a granulomatous lesion within the gut remains localized or becomes disseminated have yet to be identified.

**IBD Subdivisions**

Elucidation of the potential etiologies and pathophysiology of IBD currently attracts a great deal of research effort. In human medicine, two major subdivisions of the IBD syndrome exist:

- **Ulcerative colitis**, characterized by early crypt abscessation with neutrophils and eosinophils, followed by edema, hemorrhage, and deep accumulation of lymphocytes and plasmacytes (all confined to the mucosa and submucosa)
- **Crohn’s disease**, which is characterized by transmural granulomatous inflammation with fewer neutrophils and eosinophils than are evident in ulcerative colitis lesions

Which form of lesion develops, etiology...
notwithstanding, appears to be determined in the final analysis by whether the antigen-induced T-helper (Th) cells differentiate predominantly into the Th1 or TH2 subtype. The Th1 subtype expresses interleukin (IL)-2 and interferon-γ, which induce the granulomatous reaction characteristic of Crohn’s disease, whereas the TH2 subtype expresses cytokines IL-4, IL-5, and IL-13, which result in the less murally invasive, nongranulomatous, ulcerative, colitis-type lesion. In addition, there is evidence that mixtures of the two types of responses can occur. From our perspective, it would appear that the majority of IBD lesion types identified in horses would be more analogous to lesions seen in Crohn’s disease than in ulcerative colitis; the exception might be the lymphocytic/plasmacytic manifestation of IBD.

Inciting Factor(s)

The essential question regarding IBD focuses on identifying the factor(s) that triggers these tissue lesions in the first place. Current research results suggest two possible scenarios:

- Invasion of the submucosa and subsequent colonization of macrophages by certain bacteria (e.g., mycobacteria) that induce a Th1-type response
- Mucosal barrier disruption by any number of bacterial or parasitic enteropathogens that results in induction of an intolerance in genetically susceptible hosts to the antigens of certain bacterial species that are considered to be normal inhabitants (the autochthonous flora) of the gastrointestinal tract

In human medicine, there is great interest in the possibility (and some convincing evidence) that infection by Mycobacterium avium subspecies paratuberculosis (the cause of Johne’s disease in ruminants) may be one cause of Crohn’s disease. However, in contrast to the identification of acid-fast organisms within affected tissues in ruminants, the evidence in humans is based on polymerase chain reaction and serologic results. It has been shown under experimental conditions that horses can also be infected with M. avium subspecies paratuberculosis even by natural transmission, and a typical granulomatous enteritis was found. Acid-fast organisms could be seen in the affected tissues in the horses, and the organisms could be cultured from the feces. The organisms have yet to be identified in tissues or cultured from feces of humans with Crohn’s disease that are polymerase chain reaction–positive for M. avium subspecies paratuberculosis. To date, however, in spontaneously occurring cases of IBD in horses in which acid-fast organisms have been identified, the agent has been M. avium subspecies avium rather than paratuberculosis. M. avium subspecies avium can also cause granulomatous enteritis in humans and can be cultured from affected tissues. In humans, its most common occurrence is in immunodeficient individuals, such as those with AIDS; the immune status of affected horses has never been investigated, but by the time the problem becomes clinically apparent, the animals are undoubtedly anergic and an accurate indication of preexisting immune status would be impossible. With regard to disruption of intestinal mucosal integrity as the inducing event, there are numerous agents that affect young horses that could alter mucosal function, not the least of which include rotavirus, various bacterial enteropathogens, NSAIDs, GI parasites, and causes of gastroduodenal ulcer disease.

In my opinion, the issue of GI parasitism as an inducer of IBD is especially interesting as far as the horse is concerned and is particularly relevant to the eosinophilic form of IBD. The potential effect of migrating strongyle larvae is intriguing and, as pointed out in the Discussion section of the case report, there is at least one documented case of this causing a focal eosinophilic lesion in a horse. Why could not a diffuse reaction occur as well under certain conditions? There is precedence for this suggestion based on a report documenting such an occurrence in a group of humans exposed to a Strongyloides stercoralis hyperinfection. That said, it should be pointed out that an eosinophilic type of reaction need not be considered solely because of parasites or food intolerance, which always come to mind first, because such a reaction can be seen, for instance, in some cases of paratuberculosis in ruminants. Finally, looking at the whole parasite issue from the opposite perspective, it has been suggested that the incidence of Crohn’s disease is most prevalent in humans living in temperate regions that are highly industrialized because they have minimal or no exposure to low levels of helminthic parasite infection experienced by those living in the lesser developed regions of the world. The point here is that low-level exposure may actually promote GI tolerance to foreign antigens, perhaps in a manner similar to how Native Americans increased their skin tolerance to poison ivy by eating its leaves. This, of course, raises the question of whether very strict GI parasite control is really in a horse’s best interest.

Regarding the case at hand, it would be easy enough to consider this horse’s lesion an anomaly, considering the age of the animal and the focal nature of the lesion, were it not for the fact that a similar type of lesion has been documented in other, albeit older, horses. The fact that resection of the lesion in this and the other reported cases was all that was needed to resolve the particular problem suggests that such lesions are different in their pathogenesis than more diffuse eosinophilic enteropathies that typically cause severe weight loss, hypoproteinemia, and, in some cases, severe dermatopathy. Thus it is more likely that such lesions are due to a local insult that does not induce decreased tolerance of the gut as a whole and that the eosinophilic reaction was related to either the particular antigen involved or the species-specific propensity of the horse to mobilize eosinophils in response to any GI antigenic challenge. For instance, there are two reported cases of enteric pythiosis in a horse that caused a lesion resembling the one described in this case, in which finding the incriminating hyphae took.
some extra histopathologic effort.\textsuperscript{22,23} With that information in mind, perhaps the authors of this report might like to take another look at their biopsy specimen.

REFERENCES


