Myenteric ganglionitis as a cause of recurrent colic in an adult horse

Karen R. Blake, DVM, DACVS; Verena K. Affolter, Dr Med Vet, PhD; Linda J. Lowenstine, DVM, PhD, DACVP; Jose G. Vilches-Moure, DVM; Sarah S. le Jeune, DVM, DACVS

Case Description—A 10-year-old Lipizzaner stallion was evaluated over the course of 1.5 years because of intermittent, recurrent colic.

Clinical Findings—The horse was initially treated medically for gastric ulcers; dietary changes were made, and a deworming protocol was instituted, without resolution of colic episodes. Subsequently, the horse underwent exploratory celiotomy and a large colon volvulus was identified with diffuse colonic wall thickening. A pelvic flexure biopsy sample was submitted for histologic examination, which revealed lymphocytic (CD3-positive T cells) myenteric ganglionitis (MG). The horse developed a cecal impaction after surgery, which did not resolve, despite aggressive medical management; subsequently a complete cecal bypass was performed. Cecal and colonic wall biopsy samples were evaluated histologically and confirmed the diagnosis of MG. After surgery, the horse developed a large colon impaction, which initially responded to aggressive medical treatment, and the horse was discharged.

Treatment and Outcome—Despite rigorous feed restrictions and prokinetic and corticosteroid treatment, the horse continued to have signs of colic and was euthanized 3 weeks after discharge from the hospital because of a recurrent large colon impaction. Intestinal biopsy samples obtained at the time of death revealed chronic changes in intramural ganglia consistent with generalized MG.

Clinical Relevance—MG is a rare disease in horses, causing gastrointestinal motility dysfunction and signs of colic, which is challenging to diagnose and treat successfully. Further studies are needed to identify the etiology of this disease and to explore treatment options.

(J Am Vet Med Assoc 2012;240:1494–1500)

A 580-kg (1,276-lb) 10-year-old Lipizzaner stallion used for upper-level dressage was evaluated at the University of California-Davis William R. Pritchard Veterinary Medical Teaching Hospital with a 1.5-year history of intermittent recurrent colic. The horse had been imported from Romania 2 years prior to admission and was dewormed by the referring veterinarian routinely with various products (ivermectin, moxidectin, and pyrantel pamoate) and vaccinated regularly.

On the first visit to the Veterinary Medical Teaching Hospital, the owner reported mild colic signs (prolonged sternal recumbency, decreased appetite), which were also observed during hospitalization. Results of diagnostic testing to identify the cause of colic, including physical examination, CBC, serum biochemical analysis, examination per rectum, nasogastric intubation, abdominocentesis, abdominal radiography, and transabdominal ultrasonographic examination, were within reference limits. Gastroscopy revealed the presence of mild ulceration at the lesser curvature of the stomach adjacent to the margo plicatus. Treatment with omeprazole was initiated (4.4 mg/kg [2.0 mg/lb], PO, q 24 h for 1 month).

The horse was returned to the hospital 1 year later because of moderate signs of colic. Diagnostic testing, including gastroscopy, for colic as previously described did not reveal any abnormalities. Abdominal ultrasonographic examination revealed mild to moderate mural thickening of the small intestine (0.3 to 0.47 cm), most likely representing jejunum (reference range, < 0.3 cm). Results of a fecal McMaster quantitative egg count and indirect immunofluorescence assay for Giardia spp and Cryptosporidium spp as a possible, but unlikely, cause of enteritis in this horse were negative. During hospitalization, the horse was seen to lie down frequently; however, the owner declined further diagnostic testing and hospitalization at this time. The horse was discharged and prescribed omeprazole (2.2 mg/kg [1 mg/lb], PO, q 24 h for 1 week) to prevent ulcers from the stress of hospitalization; thereafter, omeprazole was to be administered as needed before any stressful event.

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRI</td>
<td>Constant rate infusion</td>
</tr>
<tr>
<td>EHV</td>
<td>Equine herpesvirus</td>
</tr>
<tr>
<td>MG</td>
<td>Myenteric ganglionitis</td>
</tr>
<tr>
<td>WNV</td>
<td>West Nile virus</td>
</tr>
</tbody>
</table>

From the William R. Pritchard Veterinary Medical Teaching Hospital (Blake) and the Departments of Pathology, Microbiology and Immunology (Affolter, Lowenstine, Vilches-Moure) and Surgical and Radiological Sciences (le Jeune), School of Veterinary Medicine, University of California-Davis, Davis, CA 95616. Dr. Blake’s present address is Elite Veterinary Services, 12774 Deer Mountain Blvd, No. 107, Hideout UT 84036.

The authors thank Drs. Margaret Highland, Rachel Burns, and Dennis Wilson for review of some of the biopsy samples and Drs. Michael Apumaku and Nicholas Lerche for performing the bornavirus immunohistochemical analysis.

No funding was required for this study.

Address correspondence to Dr. le Jeune (sslejeune@ucdavis.edu).
Two months later, the horse was reevaluated because of similar signs of colic. Results of physical examination, examination per rectum, CBC, serum biochemical analysis, and urinalysis were unremarkable. Results of testing of feces were negative for Clostridium difficile (antigen and toxin), Salmonella spp by culture, and Lawsonia intracellularis by PCR assay. Results of a thorough examination of the reproductive tract were within reference limits. Abdominal ultrasonographic examination revealed normal thickness of the small intestinal wall with moderate thickening of the large colon wall (0.38 to 0.52 cm) in the right cranioventral aspect of the abdomen, most likely representing either right dorsal or right ventral colon (reference range, 0.18 ± 0.04 cm). Because of the mild colitis found on ultrasonographic examination as well as the varied amounts of supplements the horse received from its owner (glucosamine, electrolytes, aloe vera juice, and various herbal supplements), it was recommended to restrict the diet to a complete pelleted feed, discontinue the supplements, and encourage pasture turnout to rest the gastrointestinal tract. It was also recommended to administer fenbendazole (7.5 mg/kg [3.4 mg/lb], PO, q 24 h for 5 consecutive days) 1 month after discharge if the horse was free of colic signs.

Seven weeks later, the horse was again referred to the veterinary medical teaching hospital because of moderate colic signs (intermittent pawing and prolonged sternal recumbency) and anorexia of 3 days duration. On physical examination, the horse’s vital signs were within reference limits, but no borborygmi could be auscultated. Examination per rectum revealed large colon in the nephrosplenic space. On abdominal ultrasonographic examination, the spleen was displaced ventrally and the left kidney could not be imaged adjacent to the spleen. Results of abdominocentesis were within reference limits. The CBC revealed elevated fibrinogen concentration (500 mg/dL; reference range, 100 to 400 mg/dL), and the serum biochemical analysis revealed mildly elevated bilirubin concentration (3.8 mg/dL; reference range, 0.5 to 2.3 mg/dL). Serum amylase and lipase activities and triglycerides and bile acids concentrations were all within reference limits.

Because of the suspicion of a nephrosplenic entrapment as well as the history of chronic colic, an exploratory celiotomy was performed. At surgery, a 360° volvulus of the large colon at the cecocolic ligament was identified and reduced by manual manipulation. Evacuation of the colonic contents via a pelvic flexure enterotomy was performed to rule out the presence of colonic enteroliths. No evidence of a nephrosplenic entrapment could be identified, but the colon wall appeared moderately thickened and an area in the dorsal aspect of the colon approximately 8 to 10 cm distal from the pelvic flexure had multiple fibrin tags with mild hyperemia on the serosal surface. A pelvic flexure biopsy sample was obtained from the pelvic flexure enteroenteritis site and submitted for histologic evaluation. No other gross abnormal findings were present.

After surgery, the horse was given IV fluids (4 mL of isotonic mixed electrolyte solution/kg/h [1.82 mL/lb/h]) and a bolus of lidocaine (1.3 mg/kg [0.6 mg/lb], IV) followed by CRI of lidocaine (0.05 mg/kg/min [0.023 mg/lb/min]) and was administered gentamicin sulfate (6.6 mg/kg [3 mg/lb], IV, q 24 h), penicillin G procaine (22,000 U/kg [10,000 mg/lb], IM, q 12 h), fluoximine meglumine (0.75 mg/kg [0.35 mg/lb], IV, q 8 h), and omeprazole (2.2 mg/kg, PO, q 24 h) because of a history of ulcers. Calcium gluconate and potassium chloride were administered in the IV fluids as indicated by changes in blood electrolyte concentrations. One day after surgery, the IV fluids and lidocaine CRI were discontinued and the feed was gradually increased to one-fourth flake (approx 0.6 kg) of grass hay every 4 hours. Antimicrobial administration was discontinued the following day.

By day 3 after surgery, the horse was comfortable but had only passed 2 piles of scant dry feces. Therefore, an examination per rectum was performed, which revealed a moderately sized cecal feed impaction. The horse was treated with 3.8 L of mineral oil via nasogastric tube, the fluoximine meglumine dose was reduced to 0.5 mg/kg (0.23 mg/lb), PO, every 12 hours to decrease the chance of providing analgesia for colic signs but maintaining anti-inflammatory properties, and feed was withheld. No change in the cecal impaction was found on examination per rectum the next day (day 4 after surgery), so the horse was again administered IV polyionic fluids at 2 mL/kg/h (0.9 mL/lb/h) and administered magnesium sulfate (363 mg/kg [165 mg/lb]) via nasogastric tube in 4 L of water. Additionally, a neostigmine CRI was initiated at 0.0022 mg/kg/h (0.001 mg/lb/h), which has been used on several occasions in horses with cecal impactions at our institution to encourage large intestinal motility without causing excessive abdominal discomfort. On day 5 after surgery, the neostigmine CRI was increased to 0.0044 mg/kg/h (0.002 mg/lb/h) and the horse subsequently passed 6 large piles of soft oily feces but also developed mild signs of colic, so the neostigmine CRI was decreased to 0.0022 mg/kg/h.

The results of histologic examination of the pelvic flexure biopsy sample were available on day 5 after surgery and revealed mild to moderate lymphocytic, eosinophilic, and plasmacytic colitis, with a predominance of the cellular infiltrate in the lamina propria and some extension into the submucosa. The serosal surface was mildly expanded by loose connective tissue. The main lesion consisted of an inflammatory infiltrate centered on the myenteric plexus, also referred to as the Auerbach plexus. Predominantly lymphocytes were observed surrounding and infiltrating the myenteric ganglia and autonomic nerves (Figure 1). The cellular infiltrate was also tracking along small intramural blood vessels. Decreased numbers of neurons were noted, interpreted as subjective neuronal atrophy. Submucosal plexuses (Meissner plexuses) were not affected. Immunohistochemistry revealed a predominance of CD3-positive T cells within the mixed CD11a-positive leukocytic infiltrate (Figure 2). These observations were consistent with a predominantly T-cell lymphocytic MG of the Auerbach plexus. Therefore, viral infections (eg, EHV, WNV, and bornavirus) were considered as possible etiologies.1–3 Results of immunostaining for WNV and bornavirus were negative. Very few EHV-positive cells were observed in the lamina propria; however, no EHV-positive cells were seen in association with the myenteric or submucosal plexuses.
On the basis of the histologic results, immune-mediated MG was considered as a presumptive diagnosis. Therefore, the horse was administered dexamethasone (0.04 mg/kg [0.018 mg/lb], IV) on day 6 after surgery after a CBC was performed, with results within reference limits. In addition, treatment with broad-spectrum antimicrobials (penicillin G procaine and gentamicin sulfate) at the prior administered doses was reinstated because of the increased risk of an incisinal infection with the horse intermittently laying in sternal recumbency and the concomitant use of an immunosuppressive dose of a corticosteroid.

Because rare EHV-positive cells were observed on immunohistochemical analysis, blood was collected for PCR diagnostic testing for EHV 1, 4, and 5; PCR diagnostic testing was also performed for WNV. Results of all tests were negative. Because of the persistence of the cecal impaction with intermittent signs of pain, despite medical and motility-modifying treatment, the need for repeated laparotomy was discussed at length with the owner, who elected to pursue medical management. Over the next 2 days, the neostigmine CRI was adjusted on the basis of the patient’s comfort level (range, 0.0022 to 0.0055 mg/kg/h [0.001 to 0.0025 mg/lb/h]) because mild colic signs were observed at the higher dose. The horse was maintained on flunixin meglumine (0.5 mg/kg, PO, q 12 h) throughout this period. The horse was also repeatedly administered intestinal laxatives and osmotic agents (mineral oil and magnesium sulfate) via nasogastric tube to rehydrate the cecal impaction, and frequent fresh grass grazing was offered to help increase gastrointestinal motility.

On day 7 after surgery, the corticosteroid was switched to prednisolone (1 mg/kg [0.45 mg/lb], PO, q 24 h) to decrease the risk of laminitis, and B-vitamin complex (10 mL) was added to the IV fluids because of decreased feed intake. On day 9 after surgery, neostigmine was discontinued and bethanecol treatment (0.35 mg/kg [0.16 mg/lb], PO, q 8 h) as well as a metoclopramide CRI (0.02 mg/kg/h [0.009 mg/lb/h]) were initiated in an effort to increase gastrointestinal motility via additional proposed mechanisms. These treatments were continued for 3 more days, and a strong recommendation was made for additional surgery. Because the cecal impaction persisted despite aggressive medical management, on day 10, the owner agreed to repeated exploratory celiotomy, intestinal biopsy, and complete cecal bypass.

Celiotomy was performed via a right paramedian incision, and the cecum was found to be fluid filled, thickened hyperemic, and filling most of the abdomen. The cecum and large colon were emptied through a typhlotomy and enterotomy, respectively. Biopsy samples were obtained from both the cecum and large colon at their respective typhlotomy and enterotomy incisions. A complete cecal bypass was performed. After surgery, the horse was maintained on a similar regi-
men as previously (penicillin G procaine, gentamicin sulfate, flunixin meglumine, lidocaine CRI, and omeprazole) with the addition of polymyxin B (2 × 10^6 U in 1 L of saline [0.9% NaCl] solution, IV, q 12 h) to treat potential endotoxemia caused by the invasive nature of the surgical procedure, and dimethyl sulfoxide (10 mL of a 90% solution in 1 L of saline solution, IV, q 12 h). Administration of neostigmine, which had previously caused the horse to intermittently develop mild signs of colic, was discontinued, and a metoclopramide CRI (0.03 mg/kg/h [0.014 mg/lb/h]) and cisapride (0.8 mg/kg [0.36 mg/lb], PO, q 8 h) were used to promote gastrointestinal motility. Prednisolone administration was temporarily discontinued at this point because of concern for decreased anastomotic healing. Blood electrolyte concentrations, PCV, total solids concentration, and venous blood gases were monitored every 6 hours, and calcium gluconate and potassium chloride were added to the fluids as necessary. An abdominal bandage was placed to protect the incision site.

The horse responded well initially after surgery and remained in the stall with no signs of discomfort. On day 1 after surgery, polymyxin B was discontinued, and 0.23 kg of a highly digestible commercial feed and 0.23 kg of grass hay pellets were added to the diet every 4 hours in an attempt to decrease bulky fiber and provide enteral nutrition. The horse remained comfortable, and on day 3 after surgery, the lidocaine CRI, metoclopramide CRI, and dimethyl sulfoxide were discontinued. Administration of penicillin was discontinued because of a procaine reaction, and cefotiofur sodium (2 mg/kg, IV, q 12 h) was administered instead.

Because the horse appeared comfortable and had an excellent appetite, IV fluid therapy was discontinued on day 3 after surgery. Feed in the form of commercial pellet and grass hay slurries was gradually increased to maintenance energy requirements, antimicrobial treatment was discontinued on day 4 after a CBC was performed and was within reference limits, and the dosage of flunixin meglumine was decreased to 0.5 mg/kg, PO, every 12 hours. The horse seemed to be doing well until the early morning hours of day 5, at which point it developed mild signs of colic and lay in sternal recumbency. An examination per rectum revealed a firm, dry impaction of the large colon with very dry feces in the rectum. For the next 18 hours, feed was discontinued and the horse was administered 6 L of enteral fluids via nasogastric tube every 2 hours with 5.3 g of NaCl, 3.8 g of NaHCO₃, and 0.4 g of KCl/L of water as well as laxatives to promote colonic hydration, as described.² By day 7, the horse had passed several piles of soft feces and again appeared comfortable.

Results of histologic evaluation of the second set of biopsy samples largely reflected features observed in the first pelvic flexure biopsy sample. In both the pelvic flexure and cecal biopsy samples, the myenteric plexus was multifocally infiltrated by lymphocytes and neuronal cell bodies were rarely observed (Figure 3). Where present, ganglion cells had degenerative changes, such as brightly eosinophilic cytoplasm and nuclear pyknosis. In the cecal biopsy sample, a moderate amount of amorphous light blue mucinous extracellular matrix was observed, occasionally surrounding the ganglia and nerves. Infrequently, there were wispy fine collagen bundles associated with the mucin. A thin layer of extracellular matrix extended between the longitudinal and circular muscle layers. Both large colon and cecum had mild, diffuse thickening of the serosa (approx 1 mm), characterized by loose fibrovascular stroma, lymphocytes, and reactive mesothelial cells. These features indicated chronic or recurring bouts of mild serosal inflammation. The latter may have been associated with repetitive handling of the intestine during surgery. The moderate plasmacellular, lymphocytic, eosinophilic, and multifocally neutrophilic colitis with edema and lymphangiectasia was similar to the lesions observed in the previous biopsy sample.

The horse was discharged on day 10 after surgery. The owner was given strict feeding instructions (a low bulk diet prescribed by a veterinary nutritionist, consisting of the commercial pelleted feed the horse had been receiving while hospitalized with grass hay, fed as a slurry). The horse was prescribed cisapride (0.8 mg/kg, PO, q 8 h) and flunixin meglumine (0.5 mg/kg, PO, q 24 h) for 3 additional days. Administration of prednisolone (1 mg/kg, PO, q 24 h) was also reinstated 1 week after discharge. Three weeks later, the horse developed signs of colic again and the referring veterinarian palpated a very firm large colon impaction per rectum. Because of the recurrence of the colic episodes and the nonresolution of the impaction with laxatives administered orally, the owner elected euthanasia. Immediately following euthanasia, the referring veterinarian

Figure 3—Photomicrograph of a large colon biopsy sample obtained from the horse in Figure 1 during follow-up celiotomy (10 days after the initial surgery). The intramural ganglion is infiltrated by small lymphocytes (arrow), and increased collagen (white arrowhead) is surrounding the ganglion and separating the intramuscular space. Remaining ganglion cells have dark eosinophilic cytoplasm, indicating degeneration (black arrowhead). H&E stain; bar = 100 µm.
ian harvested full-thickness biopsy samples from the stomach; liver; duodenum; jejunum; ileum; cecum; right ventral, left ventral, left dorsal, and right dorsal aspects of the colon; and small colon. The samples were fixed in 10% formalin and submitted to the University of California-Davis Veterinary Medical Teaching Hospital Pathology Service. Examinations of postmortem samples from the colon revealed mild portal and peritoneal hepatitis with mild bridging fibrosis. There was subcapsular fibrosis with granulation tissue and a mixed cellular infiltrate. Although gastric samples were histologically normal, minimal lymphocytic ganglionitis with loss of neuronal cells was noted in the myenteric plexus of the small intestine, particularly in the jejunum. In addition, there was a focal mild lymphocytic ganglionitis in 1 submucosal plexus. The affected submucosal ganglion still contained numerous intact neurons. Examination of the myenteric ganglia within the colon and cecum revealed vacuolar changes and lymphocytic infiltrates. Some ganglia were partially replaced by fibrous tissue and a small rim of fibrosis originating from the ganglia extended along the vasculature between the muscle layers. In several sections of the small and large intestine, the external muscle layer appeared subjectively thin, compared with the internal layer. There was a mild to moderate eosinophilic and lymphocytic infiltrate within the lamina propria and submucosa with mild fibrosis of the submucosa. Although embedded within a mixed infiltrate, the submucosal ganglia in the colon and cecum were present and appeared intact. These histologic findings indicated that the inflammatory process targeting the myenteric ganglia affected the entire intestinal tract, although it was more prominent within the cecum and large colon. The lymphoplasmacytic and eosinophilic enterocolitis was interpreted to be a sequela of the chronic obstruction. The serosa of the entire intestinal tract was multifocally thickened with mature fibrous tissue; small numbers of lymphocytes; plasma cells; a few macrophages and neutrophils; and plump reactive mesothelial cells. Both chronic inflammatory lesions of the bowel as well as repetitive handling of the intestine during surgery may have contributed to the chronic serositis. The lesions in the liver were mild, suggestive of enteropathic hepatoathy, and not considered to have been clinically relevant.

Discussion

Lymphocytic MG is a very rarely recognized gastrointestinal disorder in all species. In human patients, colonic eosinophilic MG is inapparently associated with functional intestinal obstruction.3,13 Lymphocytic ganglionitis also causes intestinal obstruction in people and is seen with paraneoplastic syndromes,3,17 autoimmune disorders such as cystic fibrosis,6 infections, and idiopathic causes.7 One postmortem study4 incidentally identified esophageal and gastric lymphocytic MG in a dog with craniospinal sensory ganglioniculitis and megasophagus, and lymphocytic MG is seen in threesus macaques experimentally infected with the simian immunodeficiency virus.10

In people, certain patients with MG seem to respond favorably to systemic corticosteroid treatment, leading to a drastic resolution of the intestinal obstruction.3,11 On the basis of those reports, corticosteroid treatment was instituted in the horse of the present report, but this was not sufficient to abolish clinical progression. Higher dosages than those that were used in the patient of the present report could have potentially positively affected the disease process, but we were reluctant to attempt this because of the potential risk of corticosteroid-induced laminitis in horses14 and the dramatic consequences of such a complication. Alternatively, treatment with other immunomodulatory drugs such as azathioprine could have been initiated, as has been successful in certain cases of eosinophilic MG in humans.3,4

Prokinetic agents were used aggressively in this horse in an effort to directly promote gastrointestinal motility through multiple pathways. However, the potential benefits of prokinetics in a patient with intestinal neuronal degeneration are debatable. Neostigmine, a cholinesterase inhibitor, was used initially to treat the cecal impaction followed by the use of betahaneol, a muscarinic cholinergic agonist.13 Both of these drugs have been shown to have significant effects on the myoelectric activity of ileum, cecum, and right ventral colon, with the net effect of hastening cecal emptying.14 A CRI of neostigmine has been used several times at our institution in an effort to promote colonic and cecal motility without causing excessive signs of abdominal pain, which is a frequent adverse effect of this drug, and the dosage is modified on the basis of the comfort level of the patient. Metoclopramide, a dopamine receptor antagonist, cholinergic agonist, and adrenergic receptor antagonist, was given as a CRI at a reduced dosage to try to minimize extrapyramidal signs often seen with the administration of this drug.13,15

The etiology of MG in horses is largely unknown. Only 1 previous case report16 documents MG with evidence of inflammation and neuronal degeneration on histologic evaluation as the cause for chronic recurrent small colon obstructions in a Standardbred mare. The authors referred to this disorder as chronic idiopathic intestinal pseudo-obstruction on the basis of a similar disorder found in humans. Recurrent inflammatory injury to the enteric nervous system was considered the etiology of altered gastrointestinal motility causing repeated small colon obstructions. Several etiologies were discussed, such as paraneoplastic visceral neuropathy, type III hypersensitivity, and a latent viral ganglionitis caused by a neurotropic virus such as herpesvirus. Although the presence of EHV, Bornavirus, and WNV could not be documented in the samples submitted from the patient of the present report, an underlying viral infection could not be completely ruled out as a potential initiating factor for the lymphocytic ganglionitis observed in this horse.17-19 An EHV infection was suggested on the basis of the presence of a small number of EHV-immunopositive cells in the lamina propria of the biopsy sample obtained during the first surgery.17 However, the positive cells were not identified adjacent to the inflammatory lesions in the ganglia, and results of a PCR assay for herpes virus were negative. Immunohistochemical analysis and PCR assay failed to document the presence of Bornavirus or WNV.18,19

Alternatively, equine dysautonomia (grass sickness)20 was considered as a possible cause for the intesti-
tinal dysfunction observed in the horse of the present report. However, grass sickness, a disorder associated with a marked decrease in intestinal neuronal density, has not yet been histologically confirmed in the United States and was therefore lower on the list of differential diagnoses. Although the horse was imported from Europe and could have been affected by the disease at that time, this was considered unlikely because the first clinical signs of colic developed approximately 6 months after its importation into the United States. In addition, acute grass sickness is characterized by dysphagia, large volumes of reflux, and reduced gastrointestinal tract motility, muscle fasciculations, and patchy sweating, all signs related to dysfunction of the autonomous nervous system, which were not observed in the patient of the present report. Moreover, most intestinal biopsy samples from horses affected with grass sickness reveal a decrease in neuronal density of both intestinal ganglia (Auerbach and Meissner plexuses), whereas in the patient of the present report, the inflammation almost exclusively targeted the myenteric (Auerbach) plexus. Furthermore, lesions identified in horses with grass sickness are mostly limited to the jejunum or ileum and degenerative changes of the ganglion cells predominated. Marked inflammation, as seen in the patient of the present report, is not a prominent feature of grass sickness. On the basis of the prolonged clinical course for this horse, chronic grass sickness had to be considered as a potential etiology. Chronic grass sickness is associated with cachexia; because of malnutrition and malabsorption, the large intestine is typically virtually empty. This is in contrast with the marked repetitive large intestinal impactions and lack of a marked weight loss observed in the patient of the present report. Moreover, there was no history of profuse reflux, dysphagia, or muscle fasciculations. Although the owner reported enhanced and prolonged sweating after work, patchy sweating unrelated to work was not observed. Unfortunately, postmortem examination in this horse was limited to the gastrointestinal tract and liver. Additional ganglia, including cervical and stellate ganglia, which are often affected in horses with grass sickness, were not available for histologic examination. Hence, chronic grass sickness, although unlikely, cannot be conclusively excluded. Schusser and White described decreased neuronal density in the myenteric plexus in the large colon of horses with acute or chronic colon obstructions. In the patient of the present report, a decrease in neuronal and myenteric plexus density was associated with inflammation targeting these structures. This supports the hypothesis of primary ganglionitis with subsequent dysfunction of the large intestine, rather than an obstruction-induced degenerative process of ganglia. In another report by Schusser et al., decreased neuron density was found in horses with chronic recurrent cecal impaction. However, there was no inflammation present surrounding the myenteric plexus in those cases, compared with the patient described in the present report, which adds further support to the diagnosis of primary ganglionitis. Ultimately, an immune-mediated process with subsequent decrease in intramural neuronal density was considered for the progressive MG seen in the horse of the present report. The trigger for the potential immune-mediated attack remains unknown. The process appeared to specifically target the myenteric plexus (Auerbach plexus; parasympathetic and sympathetic), given that submucosal ganglia (Meissner plexus; parasympathetic) were largely unaffected. Ganglion cells in the Meissner plexus mostly regulate gastrointestinal blood flow and control epithelial cell function, whereas the myenteric plexus is largely responsible for intestinal motility. Inflammation targeting the Auerbach plexus with subsequent ganglion loss explains the decrease in motility with subsequent recurrent impactions observed in the horse of the present report. The possibility of a more successful outcome in the patient described in the present report with earlier diagnosis of ganglionitis and immediate prolonged treatment with immune-modulatory medication remains unknown. The decrease in intramural neuronal density at the time of treatment made it improbable that the horse of the present report would have recovered despite aggressive corticosteroid and prokinetic treatment. Moreover, the outcome stresses the fact that intestinal biopsy is, at this time, the only tool to identify such a process and that repeated biopsy allows clinicians to monitor the progression of the disease and hence better predict the prognosis.

References