Protein-losing enteropathy caused by *Lawsonia intracellularis* in a weanling foal

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Abstract — A 5-month-old Morgan filly was presented to the Atlantic Veterinary College with a history of lethargy, fever, depression, anorexia, and dependent ventral edema. Diagnostic tests revealed severe inflammation, hypoproteinemia, and thickened small intestinal loops. Protein-losing enteropathy caused by *Lawsonia intracellularis* was diagnosed and treated successfully with erythromycin-rifampin.

Résumé — Entéropathie exudative causée par *Lawsonia intracellularis* chez un poulain au sevrage. Une pouliche Morgan de 5 mois a été présentée à l'Atlantic Veterinary College avec un historique de léthargie, fièvre, dépression, anorexie et œdème ventral déclive. Les tests diagnostiques ont révélé une inflammation importante, de l'hypoprotéinémie et un épaississement des anses du petit intestin. Une entéropathie exudative causée par *Lawsonia intracellularis* a été diagnostiquée et traitée avec succès par une association d'érythromycine-rifampicine.

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A 5-month-old Morgan filly was presented to the Atlantic Veterinary College Teaching Hospital with a 5-day history of fever (40.6°C) lethargy, depression, anorexia, decreased fecal output, and dependent edema of the abdomen. The referring veterinarian had treated her with flunixin meglumine (Banamine; Schering Plough, Pointe Claire, Quebec), and sulfadiazine trimethoprim (Tribrissen; Schering Plough), 0.5 mg/kg bodyweight (BW), IM, q12h, for 4 d. Upon her arrival, a physical examination revealed findings that coincided with those of the referring veterinarian. A complete blood cell (CBC) count showed a moderate leukocytosis (21.8×10^9/L; reference range, 6 to 12×10^9/L) with a degenerative left shift (bands 37%; reference range $< 1\%$) and a 4+ toxic change. A serum biochemical profile revealed numerous electrolyte abnormalities, including hypokalemia (2.9 mmol/L; reference range, 3.0 to 5.0 mmol/L), hyponatremia (130 mmol/L; reference range 135 to 148 mmol/L), hypocalcemia (2.12 mmol/L; reference range, 2.8 to 3.4 mmol/L), hypomagnesemia (0.49 mmol/L; reference range, 0.74 to 1.02 mmol/L), hyperphosphatemia (1.92 mmol/L; reference range, 1.0 to 1.8 mmol/L), azotemia (urea-15.2 mmol/L; reference range, 3.5 to 7.0 mmol/L), metabolic acidosis (pH 7.379), and marked hypoproteinemia (22 g/L; reference range 60 to 77 g/L). Results from a bile acid and urine analysis were within normal limits. Abdominal ultrasonographs showed abnormally thickened small intestinal walls.

Of greatest concern was the filly's hypoproteinemia. Potential causes included hepatic, enteric, and renal factors. However, hepatic and renal parameters were normal, so the hypoproteinemia was ultimately attributed to pathologic changes in the gastrointestinal (GI) tract. Differential diagnoses included immune-mediated enteritis, GI ulceration, parasitism, and neoplasia. A D-xylose absorption test was performed and its results were within normal limits. Fecal flotation revealed a 3+ ascaridiasis, and gastroduodenal endoscopy showed the presence of bots and gastric ulcers in the glandular portion of the stomach. An endoscope-guided duodenal biopsy was evaluated and found to be normal, although it was deemed to have been too superficial to be diagnostic. The owner elected to discontinue further diagnostic testing at this point, and, as no definitive diagnosis had been reached, treatment was symptomatic.

The filly was treated with 3 units of plasma; IV lactated Ringer's solution; IV sodium penicillin (Novo-Pharm, Toronto, Ontario), 4.5 million U, IV, q6h; gentocin (Gentamicin Sulfate; Veterinary Pharmacy, Guelph, Ontario), 1200 mg, IV, q24h; ivermectin (Equalan paste; Merial, Baie d'Urfé, Quebec), 0.2 mg/kg BW, PO; cimetidine (Novo-Cimetine; Novo-Pharm, Toronto, Ontario), 18 mg/kg BW, PO, q8h; and sucralfate (Novo-Sucralate; Novo-Pharm), 2 mg/kg BW, PO, q8h. Over the next 9 d, although the hypoproteinemia continued to persist, the inflammatory leukogram dramatically improved,

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the ventral edema began to resolve, and the filly's attitude and appetite improved. Her diet was supplemented with calf-starter and mare-foal ration to increase nutrient and protein intake.

Due to the suspicion of ascarid-induced immune-mediated enteritis, dexamethasone (Dexamethasone Sodium Phosphate; Vetoquinol, Lavaltrie, Quebec), 0.5 mg/kg BW, IV, q24h, was added to the therapeutic regimen once the inflammatory leukogram had returned to normal. The owners decided to take the filly home to provide her with nursing care, so antibiotics were changed to sulfadiazine trimethoprim, 30 mg/kg BW, PO, q12h; steroid therapy was changed to prednisone (Novo-Prednisone; Novo-Pharm), 1.0 mg/kg BW, PO, q12h; and the cimetidine and sucralfate regimens were continued. The attending clinician was given permission to submit a serum sample for one last attempt at a diagnosis. An indirect immunofluorescent antibody test was carried out for the detection of *Lawsonia intracellularis,* a relatively uncommon pathogen in foals. The test results were positive. The filly's antibiotic therapy was changed to erythromycin (Novo-Rythro-Estolate; Novo-Pharm), 25 mg/kg BW, PO, q8h, and rifampin (Rifadin; Hoechst Marion Roussel, Laval, Quebec), 5 mg/kg BW, PO, q8h. She recovered completely over the next few months.

Protein-losing enteropathy was the primary differential diagnosis in this case. Several conditions can lead to protein loss via the GI tract, including GI ulceration, immune-mediated enteritis, and neoplasia, as well as infectious causes such as, parasitism, *Salmonella* spp, *Ehrlichia risticii, L. intracellularis, Clostridium* spp, *Cryptosporidium* spp, *Bacteroides* spp, *Rhodococcus equi,* and others (1,2). Most of the infectious causes of foal enteritis also cause diarrhea; since this foal did not suffer from diarrhea, many of the pathogens were lower on the list of rule-outs.

Lawsonia intracellularis has only recently been identified as a potential cause of diarrhea and hypoproteinemia in horses (3–6). Infection with this pathogen is also known as proliferative enteritis/enteropathy, proliferative ileitis, and intestinal adenomatosis (3,7). Transmission of the pathogen generally occurs through the fecal-oral route (7). Proliferative enteropathy has been associated most commonly with disease in pigs, but it has also been seen affecting a variety of species, including hamsters, foxes, dogs, ferrets, rats, guinea pigs, rabbits, monkeys, ostriches, emus, sheep, deer, and, most recently, horses (3). *Lawsonia intracellularis* is an obligate intracellular bacterium that inhabits proliferating crypt cells of the small intestine, most often the ileum (3,7). Infected mucosal crypt cells undergo excessive mitotic division and contribute to a notable hyperplastic thickening and corrugated appearance of the ileal mucosa (7). As a result, mucosal villi consist of poorly differentiated crypt cells with limited brush border development and decreased absorptive capabilities (7).

Clinical signs associated with the disease include depression, weakness, ventral edema, colic, anorexia, fever, rough haircoat, diarrhea, and weight loss; the disease most commonly affects weanling foals (3). Clinical findings may include leukocytosis or leukopenia, often seen with a left shift; 3 to 4+ toxic changes to neutrophils; severe hypoproteinemia; hyperfibrinogenemia; anemia; azotemia; metabolic acidosis; electrolyte imbalances, and dehydration (3). Urinalysis and carbohydrate absorption tests are usually normal (3). Abdominal ultrasonography may reveal thickened loops of small intestine, but to arrive at a definitive diagnosis, more specific testing must be carried out. Histopathologic examination and silver staining of infected tissue, or polymerase chain reaction with affected tissue or feces from an infected animal, have been used successfully to diagnose the disease (3). Another important diagnostic tool is an indirect fluorescent antibody assay performed on serum from an infected animal (3–6). Specificity of this test is particularly high, since test results will only be positive if the animal is clinically ill. Exposure to the pathogen in the absence of disease will not elicit a detectable antibody response (7).

Due to the intracellular location of the bacterium, therapy must include an antibiotic that effectively penetrates cell membranes. Confirmed therapeutic options for treatment of proliferative enteropathy include IV fluid and electrolyte therapy, nutritional support, and erythromycin or erythromycin and rifampin therapy (3–6). Other antibiotics with promising minimal inhibitory concentration results include chlortetracycline, penicillin, enrofloxacin, and ampicillin (3,5,6). Although *L. intracellularis* has been implicated in equine GI disease only in recent years, its significance is rapidly becoming apparent and clinicians are growing more aware of its presence.

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