Therapy Protocols for Acute Hemorrhagic Diarrhea Syndrome in a Dog

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THE CASE

Rosie, a 4-year-old, 11-lb (5-kg) spayed Yorkshire terrier, is presented 12 hours after an episode of hematemesis followed by hemorrhagic diarrhea. She is hyporexic and increasingly lethargic. There is no known history of toxin exposure or dietary changes. Vaccinations, heartworm, and flea and tick preventives are current.

On presentation, Rosie is dull, tachycardic (180 bpm), and tachypneic (80 breaths per minute) with weak femoral pulses, pale pink mucous membranes, and a prolonged capillary refill time of 3 seconds. She is estimated to be 7% dehydrated. Rectal temperature is 99.1ºF (37.2ºC), and frank blood is present on the thermometer.

Physical examination findings suggest hypovolemic shock, and immediate stabilization measures are initiated. An IV catheter is placed, and a bolus of lactated Ringer's solution (LRS; 400 mL/hour [20 mL/kg IV over 15 minutes]) is administered with a fluid pump. The remainder of the physical examination is unremarkable except for mild abdominal discomfort without distension. Cardiothoracic auscultation is normal.

Abdominal radiograph and thoracic point-of-care ultrasound results are normal. Blood pressure measured via Doppler is 75 mm Hg. A blood gas and electrolyte panel reveal moderate metabolic acidosis with respiratory compensation and severe hyperlactatemia (***Table 1***, next page). Packed cell volume (PCV) and total solids (TS) are 65% and 5.5 g/dL, respectively. Electrocardiogram reveals sinus tachycardia.

What are the next steps?

THE CHOICE IS YOURS ...

CASE ROUTE 1

You suspect acute hemorrhagic diarrhea syndrome (AHDS), but the pet owner declines further diagnostics due to financial concerns and requests conservative treatment and supportive care (see next page).

CASE ROUTE 2

You suspect acute hemorrhagic diarrhea syndrome (AHDS) and pursue further diagnostics (see page 3).

CASE ROUTE 1

You initiate conservative treatment and supportive care.

Case Progression

Resuscitation with LRS (20 mL/kg IV bolus) is performed. Rosie stabilizes, and her vital signs return to normal (heart rate, 120 bpm; respiratory rate, 24 breaths per minute; blood pressure measured via Doppler, 110 mm Hg). She is hospitalized overnight, and IV fluids are administered. Fluid therapy comprises maintenance (12.5 mL/hour) and rehydration over 12 hours (350 mL dehydration deficit). Maropitant (1 mg/kg IV once) and pantoprazole (1 mg/kg IV once) are also administered. The patient is bright and adequately hydrated the following morning.

Rosie is discharged, and the owner is counseled to return to an emergency clinic if she shows inappetence for >24 hours, is dull and lethargic, or has pale gums. Omeprazole (1 mg/kg PO every 12 hours for 3 days) and maropitant (2 mg/kg PO every 24 hours for 3 days) are prescribed. The owner is instructed on how to administer LRS (30 mL/kg/24 hours SC as needed; total, 150 mL) if Rosie is unwilling to drink and has a significant amount of diarrhea. Probiotics containing multiple live bacterial strains and a bland diet are also recommended.

TABLE 1

SELECTED VALUES FROM THE BLOOD GAS & ELECTROLYTE PANEL

Value	Result	Reference Interval
PCV (%)	**65**	37-55
TS (g/dL)	5.5	5.4-7.1
pH	**7.25**	7.36 ± 0.02
Partial pressure of carbon dioxide (mm Hg)	**30**	43 ± 3
Base deficit (mmol/L)	**-3**	–1 ± 1
Bicarbonate (mmol/L)	**16**	23 ± 1
Lactate (mmol/L)	**5.6**	0.5-2
Potassium (mEq/L)	4.8	3.9-4.9
Sodium (mEq/L)	142	140-150
Chloride (mEq/L)	111	109-120
Glucose (mg/dL)	72	65-112

Values outside the reference interval are bold.

Clinical Considerations

AHDS is the sudden onset of severe bloody diarrhea with significant loss of fluid into the intestinal lumen.[1] This condition was previously known as *hemorrhagic gastroenteritis*, but a study showed no evidence of histopathologic lesions in the stomach.[2] The exact etiology of AHDS is unknown and is likely multifactorial. *Clostridium perfringens* has been suspected as a cause but can also be found in the stool of healthy dogs; most *C perfringens* biotypes are not enteropathogenic. *C perfringens* can, however, produce virulence factors that contribute to their pathogenicity.[3] Recent evidence suggests type A *C perfringens* may play a significant role in the pathogenesis of AHDS due to production of the pore-forming toxin NetF[4,5]; however, a noninvasive test to definitively diagnose AHDS does not currently exist. Diagnosis is based on clinical suspicion and exclusion of other causes of hemorrhagic diarrhea.

This patient's signalment (ie, young to middle-aged small breed dog), history (ie, peracute onset of hematemesis followed by hemorrhagic diarrhea), and elevated PCV raised suspicion for AHDS.[1,6] Elevated PCV occurs due to hemoconcentration, and concurrent loss of proteins in the GI tract results in low to normal total protein concentration. AHDS is characterized by increased vascular and GI mucosal permeability, leading to a rapid loss of fluid, electrolytes, and protein in the intestines

and possible severe dehydration and hypovolemic shock.[7]

No specific therapy for AHDS is available, and the suggested treatment is aggressive fluid therapy and supportive care. Antibiotics do not improve clinical outcome or recovery time in nonseptic patients, despite likelihood of bacterial etiology.[8,9] Disruption of the GI mucosal barrier may predispose the patient to bacterial translocation, but one study suggested there may be no significant difference in incidence of bacteremia between dogs with AHDS and healthy dogs.[10] Unwarranted antimicrobial use should be avoided to reduce the risk for antibiotic resistance and intestinal dysbiosis. In addition, antimicrobials may increase toxin release; in humans with Shiga-toxin–producing *Escherichia coli*, for example, antibiotic treatment can stimulate toxin release although there is unclear evidence supporting antimicrobial safety and efficacy.[11]

Severe intestinal mucosal damage, barrier dysfunction, and bacterial dysbiosis may be important in the pathophysiology of AHDS. Early enteral nutrition, dietary fiber, and probiotics can help restore the bacterial microbiome and intestinal barrier.[1] Probiotic treatment may be associated with an accelerated normalization of the intestinal microbiome and a shortened clinical course.[12] Although probiotics have been shown not to have a significant impact, they are unlikely to cause harm.[13]

Outcome

Rosie is anorexic over the next 24 hours, but gradually regains her normal appetite over the next 72 hours.

Choice Implications

AHDS can be fatal if untreated. Most dogs that receive aggressive therapy improve rapidly in 24 to 48 hours.[6,8] Outpatient therapy is not recommended, but minimal diagnostics and minimal hospitalization may be considered if there are financial concerns and the patient responds well to initial fluid resuscitation.

In humans, acute enteritis can trigger chronic GI disease; this may also occur in dogs.[14,15] Owners should be instructed to closely monitor for chronic or intermittent GI signs.

CASE ROUTE 2

The patient does not respond well to initial resuscitation. You pursue further diagnostics to rule out other underlying disease processes, and you administer more intensive treatment during hospitalization.

Case Progression

Initial resuscitation with LRS (20 mL/kg IV over 15 minutes) is performed. Rosie improves, but her vitals are still abnormal (heart rate, 150 bpm; respiratory rate, 52 breaths per minute; light pink mucous membranes with a capillary refill time of 2 seconds). A second bolus of LRS (20 mL/kg/15 minutes) is given. Despite mild improvement, she is still tachycardic with low to normal blood pressure (90 mm Hg) measured via Doppler. LRS (120 mL/kg/day or 25mL/hour) is continued.

Further diagnostics are performed to rule out other underlying causes for hemorrhagic diarrhea. CBC shows moderate leukocytosis characterized by neutrophilia with 5% band neutrophil concentration, hemoconcentration, and a normal platelet count. Serum chemistry profile reveals a mild to moderate ALT elevation, mildly elevated BUN and creatinine,

and severely decreased albumin (1.4 g/dL). Urinalysis reveals concentrated urine (specific gravity, 1.045); no other abnormalities are present. Basal cortisol (14 µg/dL) is elevated. Abdominal ultrasonography is performed by a board-certified radiologist; results show fluid-distended loops of intestine with no other abnormalities. A GI PCR panel for *Giardia* spp, *Cryptosporidium* spp, *Salmonella* spp, *Clostridium perfringens* enterotoxin A gene, canine enteric coronavirus, canine parvovirus 2, and canine distemper virus is ordered, but results will not be available for several days. A quantitative serum canine pancreatic lipase immunoreactivity is also performed.

After LRS (25 mL/hour) has been administered for 2 hours, PCV and TS decreased to 40% and 2.5 g/dL, respectively, canine albumin (0.8 g/kg, diluted to 5% over 6 hours; total, 4 g) is administered. Vital signs return to normal, but mentation is still dull. Heart rate is 120 bpm, respiratory rate is 24 breaths per minute, and blood pressure measured via Doppler is 110 mm Hg.

There is cardiovascular stability and adequate hydration after albumin transfusion. Hypoproteinemia-associated interstitial edema is a concern; therefore, crystalloid fluid therapy should be closely monitored. Maintenance IV fluids (12.5 mL/hour) will be continued. The fluid rate can be increased if there are significant losses (via diarrhea and vomiting). Frequently weighing the patient, urine, and feces can help guide fluid therapy.

Most patients with AHDS do not require antimicrobials, but some can become septic and should be rapidly identified.

Ampicillin/sulbactam (30 mg/kg IV every 8 hours), maropitant (1 mg/kg IV every 24 hours), pantoprazole (1 mg/kg IV every 12 hours), and buprenorphine (0.02 mg/kg IV every 8 hours) are administered. A nasogastric feeding tube is placed, and a liquid GI diet (one-third of the resting energy requirement per day) is administered via CRI and gradually increased over the next few days. The most common commercially available diet is a highly digestible, low-fat liquid diet.

Clinical Considerations

This patient did not respond rapidly to initial resuscitation; therefore, further diagnostics were performed to rule out other underlying causes of hemorrhagic diarrhea and vomiting. CBC results ruled out thrombocytopenia as a cause of GI bleeding. Hypoadrenocorticism was unlikely due to significant neutrophilia and elevated baseline cortisol. Kidney values were mildly elevated, and the urine was concentrated; therefore, azotemia was most likely prerenal in origin, and GI signs were not a result of kidney failure. Liver failure was unlikely because only ALT was moderately elevated, which was likely related to hypoperfusion of the liver. Abdominal ultrasonography was used to rule out obstruction, intussusception, and mesenteric volvulus as causes for GI signs and hypovolemia and to evaluate the pancreas while quantitative canine pancreatic lipase immunoreactivity assay results were pending. GI PCR panel ruled out infectious causes of diarrhea. A diagnosis of AHDS was most likely after other causes for hemorrhagic diarrhea and shock were excluded.

Patients with AHDS commonly have signs (eg, hypovolemia due to rapid fluid loss) of systemic inflammatory response syndrome (***Table 2***).[10] Determining whether patients are also septic can be challenging. Most patients with AHDS do not require antimicrobials, but some can become septic and should be rapidly identified. A defined a set of criteria that justify the use of antimicrobials in patients with AHDS is available (see ***Criteria for Antibiotic Administration in Septic Patients with AHDS***).[1]

Potentiated penicillins (eg, ampicillin/sulbactam, amoxicillin/clavulanic acid) are often administered as a first-line treatment for AHDS because of their broad-spectrum activity against gram-positive and gram-negative bacteria, including *Clostridium* spp.[8,9] Metronidazole may have no additional benefit in nonseptic dogs with AHDS.[16]

Because the patient in this case had severe hypoproteinemia, a colloid solution (ie, canine albumin) was administered to continue resuscitation. Canine albumin increases serum albumin concentration, colloid osmotic pressure, and blood pressure in dogs with septic peritonitis.[17] Fresh frozen plasma can also be considered. Fresh frozen plasma contains ≈30 g/L of albumin, so larger volumes are necessary to significantly increase albumin concentration.[18]

This patient was started on early enteral nutrition, which has demonstrated clinical benefit in critically ill humans and some veterinary patients.[19-21] Enteral nutrition maintains the functional and structural integrity of the intestinal epithelium and stimulates intestinal contractility.[22]

Outcome

Rosie begins to eat on her own after 3 days in the hospital, and probiotics containing multiple live bacterial strains are administered with food. IV fluid therapy is gradually tapered over the next 24 hours. IV medications are switched to oral administration, and she is discharged after 4 days. Rosie continues to eat on her own at home. Seven days after initial presentation, all medications are stopped, and Rosie has full recovery.

Choice Implications

Most patients with AHDS have a good prognosis with intensive supportive care; however, hospitalization and close monitoring are recommended for patients that develop complications (eg, severe hypoalbuminemia, bacterial translocation/sepsis, disseminated intravascular coagulation).[1]

TABLE 2

CRITERIA FOR DIAGNOSIS OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME IN DOGS[23]

Parameter	Criteria
Temperature	Small dogs (<33 lb [15 kg]): <99.5°F (37.5°C) or >102.9°F (39.4°C) Medium to large dogs (≥33 lb [15 kg]): <99.5°F (37.5°C) or >102.7°F (39.3°C)
Heart rate	>140 bpm
Respiratory rate	>20 breaths per minute
WBC	<6 or >25 × 10^3/μL; >3% band neutrophil concentration

Diagnosis requires ≥2 criteria.

CRITERIA FOR ANTIBIOTIC ADMINISTRATION IN SEPTIC PATIENTS WITH AHDS

- Systemic signs of illness that persist after volume resuscitation and supportive care
  - Dull mentation
  - Tachycardia
  - Tachypnea
  - Hypotension
- Signs of systemic inflammation at presentation
  - Rectal temperature >103.1°F (39.5°C)
  - WBC <4,000/mL or >25,000/mL
  - Band neutrophil concentration >2,500/mL
- Immunocompromised
  - Immunosuppressive treatment
  - Neutropenia
- Suspected ineffective clearance of bacteria by the liver
  - Portosystemic shunt flow
  - Liver dysfunction

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