Hepatoencephalopathy and hypocalcemia in a miniature horse mare

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A 13-year-old miniature horse mare that was 10 months pregnant had a sudden onset of dullness, inappetence, blindness, and head pressing. An equine influenza and herpes killed virus—vaccine[a] and ivermectin had been administered 2 months earlier. The mare was fed alfalfa hay and pelleted feed and had access to pasture. Of 7 miniature horses on the farm, this was the only one affected. The mare was treated wih flunixin meglumine, dipyrone, dexamethasone, and mineral oil, and was referred to the teaching hospital 6 hours after the initial observation of signs.

The mare was somnolent and obese (164 kg). She was hypothermic (36 C), but pulse and respiratory rates were normal. Mucous membranes were dry and congested, and had a prolonged capillary refill time. The mare was weak and had diffuse muscle fasiculations. The tongue protruded beyond the incisors, and the menace reflex was absent in both eyes. There was a strand of fibrin in the anterior chamber of both eyes and a corneal ulcer of the left eye. Urine dribbled continuously from the vulva, and there was symmetric distention of the abdomen, consistent with a 10-month-old fetus.

Complete blood count results were normal. Serum biochemical analysis revealed azotemia (2.3 mg/dl of creatinine/dl; normal, 0.6 to 1.8 mg/dl), hypocalcemia (7.7 mg/dl; normal, 10.7 to 13.4 mg/dl), hyponatremia (130 m*M*; normal, 132 to 141 m*M*), hypochloremia (86 m*M*; normal, 94 to 102 m*M*), and hyperglycemia (419 mg/dl; normal, 72 to 114 mg/dl). Venous blood gas analysis revealed acidosis (pH 7.23; normal, 7.35 to 7.45), low bicarbonate concentration (13.9 m*M*; normal, 22 to 26 m*M*), and low PCO_2 (32.4 mm of Hg, normal, 40 to 45 mm of Hg).

The mare was treated with a continuous intravenous infusion of Ringer solution supplemented with calcium gluconate,[b] an isotonic solution of sodium bicarbonate, sodium ampicillin (20 mg/kg of body weight, IV, q 6 h) and flunixin meglumine (0.25 mg/kg, IV, q 6 h). Atropine and an ophthalmic antibiotic ointment were placed on both eyes every 6 hours. The urinary bladder was catheterized and decompressed every 12 hours.

The next morning the mare was dull and appetent and yawned frequently. The menace reflex was present in both eyes. The mare was stronger and there were no muscle fasiculations. The temperature, pulse, and respiratory rates were normal. The mare dribbled urine intermittently.

A CBC revealed mature neutrophilia (8,736/μl; normal, 2,500 to 7,500/μl), immature neutrophilia (312/μl; normal, 0 to 100/μl), lymphopenia (1,352/μl; normal, 1,500 to 2,500/μl), and hypofibrinogenemia (100 mg/dl; normal, 100 to 400 mg/dl). Serum biochemical analysis revealed hypocalcemia (9.8 mg/dl), hyperglycemia (236 mg/dl), hyperbilirubinemia (3.0 mg/dl; normal, 0.1 to 1.9 mg/dl), hyperammonemia (44 μ*M*; normal 11 to 44 μ*M*), and high alkaline phosphatase (480 IU/L; normal, 109 to 315 IU/L) and sorbitol dehydrogenase (35 IU/L; normal, 1.9 to 5.0 IU/L) activities. Results of venous blood gas analysis, prothrombin time, and partial thromboplastin time were normal. Urinalysis revealed a specific gravity of 1.028, aciduria (pH 5.0), proteinuria (trace), glucosuria (500 mg/dl), and a large amount of blood. The urine sediment had a high number of erythrocytes (10 to 12/field; 450×). The mare was treated as before except the intravenous infusion of sodium bicarbonate was discontinued.

The mare's attitude, appetite, and body weight were reduced (body weight by 3 kg) during the next 2 days. There was no fibrin seen in the anterior chamber of either eye, and the corneal ulcer on the left eye was smaller. The mare was urinating normally. Results of a CBC were normal. Serum biochemical analysis revealed hypernatremia (145 m*M*); hyperchloremia (111 m*M*); hyperbilirubinemia (2.0 mg/dl); hyperammonemia (60 μ*M*); high alkaline phosphatase (721 IU/L), sorbitol dehydrogenase (45 IU/L), and aspartate transaminase (667 IU/L; normal, 205 to 255 IU/L) activities; low BUN concentration (7.0 mg/dl; normal, 8 to 27 mg/dl);

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[a]Fluvac-EHVI (lot No. 1592066), Fort Dodge Co, Fort Dodge, Iowa.

[b]Cal-nate, Butler Co, Columbus, Columbus Ohio.

and hypoglycemia (68 mg/dl). Urinalysis revealed specific gravity of 1.025, aciduria (pH 5.5), proteinuria (trace), ketonuria (trace), and bilirubinuria (trace). Ultrasonographic examination of the abdomen revealed a live fetus and a normal-appearing liver. A percutaneous biopsy of the liver was performed, and tissue was submitted for histologic examination. The mare was treated with continuous intravenous infusion of a solution of half-strength Ringer and 2.5% dextrose, and B-complex vitamins. Administration of sodium ampicillin, flunixin meglumine, and ophthalmic medications was continued. Catheterization of the urinary bladder was not required.

The mare's attitude, appetite, and body weight improved (body weight by 3 kg) during the next 3 days. The corneal ulcer of the left eye was healed. Results of a CBC and urinalysis were normal. Serum biochemical analysis revealed hyperammonemia (50 μM) and high alkaline phosphatase activity (492 IU/L). Histologic examination of the liver biopsy specimen revealed numerous small areas of acute hepatitis characterized by neutrophil infiltration and hepatocyte degeneration. There was mild to moderate, diffuse intracellular vacuolation of hepatocytes. Administration of all medications was discontinued, and the mare was discharged from the hospital 9 days after admission.

The mare was reported to be alert and appetent 1 week later. Serum biochemical analysis performed at that time revealed high alkaline phosphatase activity (631 IU/L). The mare foaled without complications 1 month later, and the mare and foal were reported to be doing well.

Hypocalcemia develops infrequently in horses and often is associated with lactation, exertion, or prolonged transportation.[1-3] However, a horse may be hypocalcemic without a predisposing cause.[4-6] Hypocalcemia does develop commonly in draft horses and ponies.[1-3,6] We have observed hypocalcemia in other miniature horses with gastrointestinal disorders.

Clinical signs of hypocalcemia depend on the serum concentration of ionized calcium.[3,7] Mild hypocalcemia is associated with hyperexcitability.[3] The clinical findings of moderate hypocalcemia usually are observed and include stiffness, incoordination, tachypnea, dyspnea, muscle fasiculations, trismus, salivation, dysphagia, tachycardia, arrhythmia, and synchronous diaphragmatic flutter.[1-6] Severe hypocalcemia is associated with recumbency, convulsions, and death.[3,7] The weakness, muscle fasiculations, hypothermia, and urinary incontinence in the mare of this report likely was associated with moderate hypocalcemia. These clinical signs were absent 36 hours after beginning the intravenous administration of an infusion supplemented with calcium when the concentration of serum calcium was normal.

The measured serum calcium concentration includes chelated, protein-bound, and ionized calcium.[7] The chelated and protein-bound calcium are inactive, compared with the ionized calcium.[7] Acidemia favors the ionization of calcium, whereas alkalemia favors the binding of calcium.[7] The signs of hypocalcemia in this mare likely would have been more severe if she did not have acidemia.

The clinical signs of hepatic insufficiency develop when most hepatic function is lost and include dullness, inappetence, weight loss, encephalopathy, icterus, photodermatitis, and coagulopathy.[7,8] The signs of hepatic encephalopathy are suggestive of cerebral dysfunction and include somnolence, yawning, ataxia, head pressing, circling, blindness, seizures, and coma.[7-13] The signs of hepatoencephalopathy in this mare, including dullness, somnolence, blindness, head pressing, and yawning, were progressively less intense after admission and suggested improved hepatic function.

Hyperammonemia, hypoglycemia, decreased serum concentration of branched chain amino acids and increased serum concentration of aromatic amino acids have been associated with hepatoencephalopathy.[7,8,11,12] The signs of hepatoencephalopathy in this mare were most prominent within 12 hours of her admission. The mare was hyperglycemic at admission, likely from the dexamethasone injection or endogenous glucocorticoid release. There was no exacerbation of signs of hepatoencephalopathy when the mare was hypoglycemic, 36 hours after admission. The mare had mild hyperammonemia 12 hours after admission, but the signs of hepatoencephalopathy were substantially reduced when the highest concentration of serum ammonia was recorded 60 hours after admission. There was no correlation between the severity of signs of hepatoencephalopathy, and hypoglycemia or hyperammonemia in this case, and in another report.[14] Analysis of amino acids in serum was not performed in the mare of this report.

Icterus is caused by an accumulation of bilirubin.[7] Icterus is a common sign of hepatic insufficiency and usually develops when the serum concentration of total bilirubin exceeds 3 mg/dl.[8] There was no icterus detected in this mare, although the peak concentration of total bilirubin in the serum was 3.8 mg/dl, 36 hours after admission. The degree of icterus is influenced by the concentrations of conjugated and unconjugated bilirubin in serum,[8] which were not measured in the mare of this report.

The liver is essential for metabolism, detoxification, and excretion of a variety of toxic products of digestion.[8] Endotoxin may enter the general circulation of an animal with severe hepatic insufficiency, inducing clinical signs of endotoxemia.[11] The dullness, inappetence, congested mucous membranes, metabolic acidosis, and strand of fibrin in both eyes in this mare may have been associated with endotoxemia. These clinical signs improved progressively after intravenous treat-

ment with fluids, an antimicrobial, and an anti-inflammatory drug.

To our knowledge, the clinical signs of hepatoencephalopathy and concurrent hypocalcemia have not been reported in horses. Hypoalbuminemia has been reported in horses with hepatic insufficiency[7,8,14] and may result in hypocalcemia.[7] However, there usually are no signs of hypocalcemia because the serum concentration of ionized calcium is normal.[7] The concentration of serum albumin in this mare was normal.

The serum calcium pool is in a dynamic state, and calcium homeostasis is dependent on many factors including diet, pregnancy, and function of the intestine, kidneys, and bone.[7] Many minerals and hormones are responsible for the maintenance of normocalcemia.[7] The cause of hypocalcemia in this mare is unknown. We suspect that, in this mare, hepatic insufficiency reduced appetite and homeostatic mechanisms responsible for normocalcemia, and with the continued demand for calcium by the fetus, resulted in hypocalcemia.

The diagnosis of hepatic disease in this mare was suspected from the clinical signs of encephalopathy and abnormal results of serum biochemical analysis, and it was confirmed by histologic examination of the liver. Many causes of acute hepatic necrosis have been reported in horses, including serum hepatitis, *Bacillus piliformis* infection, iron intoxication, and toxins in plants and molds.[7-13] The cause of acute hepatic necrosis in this mare is unknown, but the administration of a vaccine prepared from equine tissue 2 months earlier suggests that serum hepatitis likely was the cause.

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Book Review: Women in Veterinary Medicine: Profiles of Success

As our profession undergoes a transition to a more diverse population, Drs. Drum and Whiteley have written *Women in Veterinary Medicine* at a time when it is most needed. The authors examine the lives and profiles of 20 successful women veterinarians. These vignettes are inspiring, personal, often poignant, and always insightful. The reader is struck by the extraordinary professional achievements attained by these women, especially as their personal lives and backgrounds are expertly interwoven into their stories and shared with the reader.

These veterinarians represent lessons in courage and self-determination. Their personal setbacks, including their experiences of discrimination, strengthened their resolve to excel in veterinary medicine. These women have strong nurturing and caring traits that are transferred into their professional endeavors. At a time when changing social values demand an evolution of veterinary medicine, these traits are invaluable.

This book, albeit somewhat fragmented, is a great read; not only can readers appreciate the success and accomplishment of 20 professional leaders, but they also can identify and appreciate their very human qualities, sensitivities, and even vulnerabilities. The 20 veterinarians are responsible to their gender, but even more responsible to the society that we all serve.

This book should prove enjoyable and inspiring for other women veterinarians who may want to learn of these profound and often pioneering efforts. For all veterinarians, the book can be insightful and should lead to a better understanding of a female perspective of veterinary medicine and gender-derived problems. Yet, most importantly, our entire profession can be proud and hopefully be moved to greater accomplishments because of these success stories. I highly recommend this Iowa State Press book and compliment its talented authors.—[*Women in Veterinary Medicine: Profiles of Success. By Sue Drum and H. Ellen Whiteley. 286 pages. 1991. Iowa State University Press, Ames, IA 50010. Price $27.95.*]—LONNIE J. KING