Intermittent hypoglycemia in a horse with anaplastic carcinoma of the kidney

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A 14-year-old Mustang gelding was referred to the University of California, Davis, Veterinary Medical Teaching Hospital for evaluation of a suspected episode of hypoglycemia and collapse. The horse had a 5-day history of mild colic and partial anorexia, chronic diarrhea of unknown duration, and a 2- to 3-week history of weight loss despite an increase in the amount of feed. On the morning of referral, the horse was examined by the referring veterinarian who reported that the horse was recumbent with hypoglycemia. At that time, the horse responded to IV administration of flunixin meglumine and dextrose and was standing and eating within a few minutes after treatment.

On initial examination at the veterinary teaching hospital, the horse was observed to be moderately thin and appeared slightly weak with noticeable muscle tremors. Temperature, heart rate, and respiratory rate were normal, and the horse passed soft formed feces followed by fluid feces during the examination. Examination per rectum did not reveal any clinically important abnormalities. Blood glucose concentration was 185 mg/dl (reference range, 59 to 122 mg/dl). Urine glucose concentration was initially estimated to be 230 mg/dl by use of a dipstick test, but results of a follow-up test approximately 24 hours later were negative. Total WBC count, PCV, and serum total protein, sodium, potassium, ionized calcium, and bicarbonate concentrations were within reference limits.

Abdominocentesis yielded a hazy yellow fluid with a total protein concentration of 1.2 g/dl and WBC count of 690 cells/µl. Evaluation of blood samples collected on days 3, 4, and 10 of hospitalization revealed moderate anemia (PCV = 22.5; 28.6, and 24.9%, respectively) and mild thrombocytopenia (98,000 platelets/µl) on day 3. Serum glucose, electrolyte, urea nitrogen, creatinine, total bilirubin, albumin, and globulin concentrations and sorbitol dehydrogenase, r-glu-

tamyltransferase, aspartate aminotransferase, alkaline phosphatase, and creatine kinase activities were within reference ranges the morning following admission.

Initially, financial constraints of the owner prevented thorough diagnostic evaluation, and the horse was treated conservatively on the basis of an assumption that it had colic of an unknown cause that was resolving. On the third day of hospitalization, the horse developed a large abscess on the left side of the neck consistent with infection of the site where the owner had injected flunixin meglumine multiple times during the week prior to admission. Bacterial culture of material from the abscess yielded Bacillus cereus, which was resistant to penicillin but susceptible to gentamicin. The abscess responded to treatment with gentamicin IV, hot packing, and drainage by needle aspiration and decreased in size considerably during the remaining 14 days of treatment. As the horse did not initially have any signs of acute illness following admission, treatment of this abscess was the reason for the prolonged hospitalization.

On the eighth day of hospitalization, the horse was found to be nonresponsive. It was standing but would not move, even when encouraged, or respond when offered food. Its pupils were dilated and did not respond to light, and its ears were twitching repetitively. Heart and respiratory rates were within reference limits. Blood glucose concentration was 13 mg/dl. The horse collapsed during examination, and 5 L of lactated Ringer’s solution with 10% dextrose was administered IV. The horse responded almost immediately and was standing and eating within 10 minutes after initiation of IV treatment. Blood glucose concentration was 296 mg/dl following administration of 5 L of lactated Ringer’s solution with 10% dextrose.

Blood glucose concentration was monitored 1 to 3 times daily for the remaining 8 days of hospitalization. Nine of 12 samples had a blood glucose concentration between 63 and 136 mg/dl, and 3 had a concentration between 37 and 53 mg/dl. Blood glucose concentration was not obviously associated with time of blood sample collection or time since the horse was fed. For 3 samples, serum insulin concentration was measured at the same time blood glucose concentration was measured. For the first sample, insulin concentration was < 1.5 µU/ml (reference range, 1 < 300 µU/ml), and glucose concentration was 37 mg/dl. For the second sample, insulin concentration was 65.6 µU/ml, and glucose concentration was 136 mg/dl. For the third sample, insulin concentration was 14.6 µU/ml, and glucose concentration was 37 mg/dl. Insulin-to-glucose ratios for samples 1, 2, and 3 were 0.4, 0.48, and 0.4, respectively, which were within the range previously documented for healthy adult horses.2 Other than the episode of hypoglycemia on the eighth day of hospitalization, the horse had no clinical signs of disease. The horse was treated conservatively, and the abscess was allowed to resolve without treatment. The horse was discharged after 14 days of treatment. As the horse did not initially have any signs of acute illness following admission, treatment of this abscess was the reason for the prolonged hospitalization.
Hypoglycemia in horses with colic associated with hyperlipidemia syndrome or in the terminal stages of enteritis or acute endotoxemia, and in ponies with prolonged exercise, in horses with acute toxic injury, and in horses that are exhausted following extensive exercise. Hypoglycemia in adult horses.

It seems that few of the diseases known to induce hypoglycemia. This is apparently not attributable to the unique carbohydrate metabolism in horses; rather, the rapid decrease in blood glucose concentration, coupled with the apparent lack of an insulin-like growth factor (IGF)-II, referred to as “big IGF-II,” and an alteration of its interactions with other substances. In humans with hypoglycemia secondary to non–insulin-secreting tumors, there is impaired formation of serum complexes of IGF, IGF-binding protein, and the acid-labile subunit. These patients have high circulating concentrations of big IGF-II (which has insulin-like activity), may have normal or high concentrations of normal IGF-II, and have normal or low insulin concentrations. The result is increased insulin-like activity and uptake of glucose into tissues, primarily muscle, resulting in hypoglycemia. Serum big IGF-II concentration returns to normal and, as in dogs, hypoglycemia resolves following complete surgical removal of the tumor. Other proposed causes of tumor-associated hypoglycemia include increased metabolic demand for glucose by the tumor itself, stimulation of increased glucose uptake by tumor necrosis factor, and in the case of neoplasia involving the liver, decreased hepatic gluconeogenesis because of a decrease in the total number of functional hepatocytes.

It is possible that hypoglycemia in the horse described in the present report resulted from tumor-related production of big IGF-II. Although the horse had intermittent signs of mild colic and diarrhea, there was no evidence of endotoxemia, strangulation of the intestines, starvation, excessive exercise, or hyperlipidemia. Histologic examination of the tumor, serum insulin concentration, and the insulin-to-glucose ratio, which was evaluated on 3 separate occasions, did not support a diagnosis of an insulin-secreting islet cell tumor.

The horse did have moderate multifocal hepato-cellular necrosis and biliary hyperplasia, but most of the liver was unaffected histologically. Serum albumin and bilirubin concentrations and hepatic enzyme activities were normal, and the horse did not have any other clinical or laboratory evidence of compromised liver function. In addition, episodes of hypoglycemia were sporadic, and the horse had blood glucose concentrations within reference limits most of the time. Thus, it is unlikely that persistent hepatic disease or dysfunction was a major contributor to the hypoglycemia. Rather, the rapid decrease in blood glucose concentration, coupled with the apparent lack of an
association between blood glucose and insulin concentrations, was suggestive of intermittent action of a substance with hypoglycemic or insulin-like activity in this horse.

To our knowledge, there has been only 1 other report of hypoglycemia associated with a nonislet cell tumor in a horse.11 This paraneoplastic condition may be more common in horses than presently recognized, and neoplasia should be included in the differential diagnosis for horses with hypoglycemia.

References