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Anesthesia Case of the Month

History

A 22-year-old 583-kg (1,283-lb) Quarter Horse gelding was referred to the William R. Pritchard Veterinary Medical Teaching Hospital for evaluation of right forelimb lameness. On the basis of patient history and clinical examination findings, a radiographic study of each carpus was performed. After discussion with the owner regarding further diagnostic and treatment options, CT of the right carpus was elected to better characterize the extent of injury to the carpus, followed by carpal arthroscopy if indicated. Prior to anesthesia, a CBC and serum biochemical analyses were performed, with the only abnormality being mild hyperglycemia (135 mg/dL; reference range, 50 to 107 mg/dL).

The following day, general anesthesia was induced and CT was performed. Food but not water was withheld for approximately 8 hours prior to anesthesia. A 14-gauge, 5.25-inch polyurethane catheter was placed in the left jugular vein with standard aseptic technique. Thirty minutes prior to induction of anesthesia, the horse was premedicated with penicillin G procaine (22,000 U/kg [10,000 U/lb], IM), gentamicin sulfate (6.6 mg/kg [3.0 mg/lb], IV), phenylbutazone (4.4 mg/kg [2.0 mg/lb], IV), and tetanus toxoid. The horse was then sedated with xylazine hydrochloride (1.1 mg/kg [0.5 mg/lb], IV) and morphine sulfate (0.1 mg/kg [0.05 mg/lb], IV). Anesthesia was induced by means of IV administration of a combination of ketamine hydrochloride (2.2 mg/kg [1.0 mg/lb]) and midazolam hydrochloride (0.05 mg/kg [0.023 mg/lb]). Following induction of anesthesia, orotracheal intubation was performed, and the horse was mechanically ventilated,[a] with general anesthesia maintained with delivery of isoflurane in oxygen. A continuous infusion of crystalloid IV fluids was administered for the duration of general anesthesia (total volume, approx 4 L). Indirect blood pressure (measured with oscillometry), heart rate and rhythm (measured with a lead II ECG), arterial oxygen saturation (measured by means of pulse oximetry), respiratory rate, end-tidal carbon dioxide concentration (measured with capnography), and end-tidal isoflurane concentration were monitored throughout with a multiparameter monitor.[b] No cardiovascular or respiratory abnormalities were observed.

Mean arterial pressure remained between 90 and 110 mm Hg throughout the anesthetic episode, without inotropic support. Heart rate ranged from 35 to 40 beats/min for the duration of the anesthetic episode. Because of the expected brevity of the procedure, arterial blood gases were not measured.

The horse was positioned in right lateral recumbency on a custom-built CT table,[c] and 0.6-mm contiguous images of the carpus were obtained, with image acquisition extending from the distal portion of the radial diaphysis to the proximal diaphysis of the third metacarpal bone.[d] On the basis of results of CT imaging, the expected benefits of arthroscopy were deemed minimal, and it was elected to recover the horse from general anesthesia and pursue medical management. The time from induction of anesthesia to moving of the patient into the recovery stall was 40 minutes. The horse was placed in right lateral recumbency in a 2.4 × 3.0-m recovery stall, with a padded leather helmet secured to the head and neoprene boots placed on all 4 limbs. Once spontaneous breathing was observed, romifidine (0.002 mg/kg [0.0009 mg/lb], IV) was administered, and oxygen supplementation (via nasal tube) commenced at a flow rate of 10 L/min.

Within 5 minutes of being placed in the recovery stall, the horse made several unsuccessful attempts to stand, characterized by explosive behavior, marked incoordination, and ataxia. The horse eventually stood without assistance 20 minutes after being placed in the recovery stall and remained there for an additional 30 minutes, during which time the incoordination and ataxia resolved. The horse was walked back to its hospital stall and was noted to be quiet, alert, and responsive, with no injuries or increase in lameness identified secondary to the difficult recovery from anesthesia. However, generalized marked perspiration was noted as the horse was being walked from the recovery stall to the hospital stall. This was attributed to the multiple attempts made by the horse to stand during recovery from anesthesia. Although the horse was maintained in a climate-controlled environment (22.2°C [72°F]) for the duration of the anesthetic episode, it was possible that outdoor temperature was a contributing factor, as temperatures were in excess of 32.2°C (90°F). The horse was subsequently rinsed with cool water and dried immediately prior to being returned to the stall. After being returned to the stall, the horse stood quietly for approximately 30 minutes before briefly circling in the stall and collapsing into left lateral recumbency. The total time from discontinuation of anesthesia to collapse was approximately

This report was submitted by Scott A. Katzman, DVM; Marcos Perez-Noguez, LV, MSc; Bruno H. Pypendop, Dr Med Vet, Dr Vet Sci; Charles E. Alex, DVM; and Verena K. Affolter, Dr Med Vet, PhD; from the Department of Surgical and Radiological Sciences (Katzman, Pypendop), the William R. Pritchard Veterinary Medical Teaching Hospital (Perez-Noguez), and the Department of Pathology, Microbiology and Immunology (Alex, Affolter), School of Veterinary Medicine, University of California-Davis, Davis, CA 95616.

Address correspondence to Dr. Katzman (sakatzman@gmail.com).

80 minutes. Vital parameters at that time, the first obtained following recovery from anesthesia, were indicative of severe hypotension, evidenced by an auscultated heart rate of > 120 beats/min; a weak, rapid peripheral pulse palpable at the level of the facial artery; white mucous membranes; and lack of capillary refill. Respiratory rate was not measured, although bilateral nasal airflow without evidence of upper airway obstruction was noted.

Results of a venous blood gas analysis included marked decreases in pH (7.095; reference range, 7.32 to 7.44), HCO_3^- (11.8 mmol/L; reference range, 20 to 28 mmol/L), and base excess (–16 mmol/L; reference range, –2 to 2 mmol/L) and an increase in plasma lactate concentration (30 mmol/L; reference range, < 2.0 mmol/L). Findings were indicative of severe tissue hypoxia suspected to be secondary to hypovolemic shock, although the cause had not yet been identified. Because of the rapid deterioration of the horse's condition, time did not permit further objective diagnostic evaluation to be performed.

Initial treatment consisted of nasal oxygen supplementation at a flow rate of 10 L/min and administration of hypertonic saline solution IV. However, despite these supportive and resuscitative efforts, the horse died within 10 minutes after collapse.

Question

What was the cause of postanesthetic death in this patient? What nonspecific antemortem findings may have been indicative of this condition, potentially allowing for earlier intervention?

Answer

The cause of death in this patient was hypovolemic shock secondary to marked retro- and intraperitoneal hemorrhage from a ruptured adrenal gland neoplasm identified on postmortem examination. Immunohistochemical staining with anti-chromogranin A antibody[e] (antibody dilution, 1:300) and anti-synaptophysin antibody[f] (antibody dilution, 1:80) was performed on 4-µm-thick sections of paraffin-embedded tissue sections. Results of histopathologic and immunohistologic (tumor cells expressed chromogranin A and synaptophysin) examination confirmed a diagnosis of pheochromocytoma.[1]

Nonspecific antemortem signs that may have been associated with catecholamine release from the tumor included hyperglycemia identified on the preoperative serum biochemical analysis, maintenance of adequate blood pressure while anesthetized with isoflurane without the administration of an inotrope, and profuse sweating following recovery from anesthesia. However, because neither catecholamines concentrations nor concentrations of their metabolites were measured on hematologic evaluation during the anesthetic episode, this association could not be proven.

Discussion

Pheochromocytoma is an infrequently diagnosed neoplastic condition in horses with a prevalence of 0.95% in horses undergoing necropsy in 1 report.[2] Pheochromocytomas develop from the chromaffin cells of the medulla of the adrenal gland and have been diagnosed in a wide variety of domestic animals.[1–3] Most commonly, horses are evaluated for signs of abdominal discomfort,[2,3] and in 1 study,[3] serum biochemical abnormalities and nonspecific clinical signs included hyperglycemia and profuse sweating in 4 of 10 horses. In the horse of the present report, mild hyperglycemia was noted on results of preanesthetic laboratory testing, but because glucose concentrations continually fluctuate in response to diet and physiologic conditions in healthy horses,[4] this finding was considered to be associated with the stress of hospitalization. In human patients and dogs with pheochromocytomas, hypertension has been documented as a clinical feature secondary to catecholamine release.[5,6] It is common for horses undergoing anesthesia with inhalant anesthetics to require inotropic support to maintain mean arterial pressure > 70 mm Hg.[7] In the horse of the present report, it is of note that intraoperative inotrope administration was not necessary, although this may or may not have been related to catecholamine release from the pheochromocytoma. There was no history of excessive sweating in this horse. Excessive sweating noted after recovery from general anesthesia was attributed to the behavior exhibited by the horse during the recovery phase of anesthesia. A retrospective study[2] reported tachycardia in 7 of 7 horses and hemorrhagic shock as a result of hemoabdomen in 4 of those 7 horses, for which pheochromocytoma was considered to have contributed to clinical signs and death. Similar terminal clinical signs and subsequent necropsy findings were identified in the horse described in the present report.

In a large epidemiological multicenter study[8] evaluating perioperative equine fatalities, including 41,824 cases over a 6-year period, the rate of non–colic-related anesthetic-associated death was reported to be 0.9%, with 1.2% of deaths related to postoperative hemorrhage and 4.6% of horses found dead postoperatively. Additionally, horses > 14 years of age were at a significantly greater risk for anesthetic-associated death. Although that study did not specifically address the sources of postoperative hemorrhage or the final diagnosis for horses found dead, none of the included horses were reported to have died secondary to development of hemoabdomen, a neoplastic process, or a combination of the 2.

Both assisted recovery and unassisted recovery from general anesthesia were employed at our institution at the time of this horse's death, with the decision dependent on temperament of the horse, duration of anesthesia, and surgical or diagnostic procedure being performed and

the final decision made by the attending anesthesiologist and surgeon. In the case described here, unassisted recovery was elected primarily on the basis of the short duration of anesthesia. Moreover, prior to anesthetic induction, the horse appeared to be healthy on the basis of results of a physical examination and preoperative hematologic and serum biochemical testing.

Because no fluctuations in cardiovascular parameters indicating the development of hypovolemia were observed during anesthetic monitoring, we suggest it was likely that intra-abdominal hemorrhage began during recovery from anesthesia for the patient of this report. This may have been a result of blunt abdominal trauma experienced during the initial explosive unsuccessful attempts to stand. However, because the patient underwent indirect monitoring of blood pressure, there could have been fluctuations in blood pressure that may not have been observed. Direct blood pressure monitoring in this case would have been more reliable in detecting changes indicative of an adverse event during the anesthetic episode, as it is the most accurate and sensitive method available.[9]

There have been sporadic reports in the scientific literature of hemorrhage occurring secondary to blunt trauma in human patients with pheochromocytomas. Coincidentally, 2 cases reported[10,11] involved horses. In one,[10] an individual fell from a horse, and in the other,[11] a horse kicked the individual in the torso. The individual who fell survived her injuries, and the individual who was kicked died despite similar case management, including multimodal imaging of the abdomen, aggressive supportive care, and repeated laparotomy. Although resuscitative measures were immediately instituted in the case reported here, it was unlikely that this horse could have survived, given the extent of intra-abdominal hemorrhage, subsequent hypovolemic shock, and limitations associated with implementing successful cardiovascular resuscitation in horses (specifically, the limited ability to deliver rapid IV volume expansion to equine patients).

To our knowledge, this is the first report of postanesthetic death in a horse associated with intra-abdominal hemorrhage from an occult pheochromocytoma. Although rare, hemoabdomen secondary to a neoplastic process should be considered in the differential diagnosis for horses that have been found dead or that died acutely in the immediate postanesthetic period.

Footnotes

a. 2800C Large Animal Anesthesia Ventilation System, Mallard Medical Inc, Redding, Calif.
b. Datex-Ohmeda AS/5 Anesthesia Monitor, GE Healthcare, Chicago, Ill.
c. Large Animal Peters Carbon Fiber CT Table, Kimsey Welding Works, Woodland, Calif.
d. GE Lightspeed 16-Slice CT Scanner, GE Medical Systems, Waukesha, Wis.
e. NB100-79914, Novus Biologicals, Littleton, Colo.
f. M0776, Dako, Carpinteria, Calif.

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