Anesthesia Case of the Month

History

A 4-year-old 490-kg (1,080-lb) American Saddlebred gelding was referred to the University of Georgia Veterinary Teaching hospital for treatment of colic of approximately 24 hours' duration. The horse had initially been treated with flunixin meglumine, acepromazine, and probiotics by the trainer, the referring veterinarian, who examined the horse the following day because it still had signs of pain, administered detomidine and flunixin meglumine. Rectal examination at this time revealed distension of the large colon, and the horse was referred to the Veterinary Teaching Hospital because of ongoing signs of pain.

On initial physical examination, the horse's heart rate was high (52 beats/min). Rectal temperature (37.5°C [99.5°F]), respiratory rate (16 breaths/min), capillary refill time (<2 seconds), and mucous membranes (pink and moist) were unremarkable, and no gastric reflux was obtained. Rectal palpation revealed loose feces with a gas-distended large colon, small colon impaction, and distension of the small colon with hairpin-like turns. The PCV (36%) and total solids concentration (7.1 g/L; reference range, 2.9 to 4.5 mmol/L; reference range, 2.9 to 4.5 mmol/L), hyperglycemia (181 mg/dL; reference range, 64 to 132 mg/dL), and mild hypokalemia (2.8 mmol/L; reference range, 21 to 29 mmol/L) were noted. Blood flow was increased to 140, 90, and 104 mm Hg 5 minutes after administration of detomidine and probiotics by the trainer; the referring veterinarian, who examined the horse the following day because it still had signs of pain, administered detomidine and flunixin meglumine. Rectal examination at this time revealed distension of the large colon, and the horse was referred to the Veterinary Teaching Hospital because of ongoing signs of pain.

The PCV (36%) and total solids concentration (7.1 g/L) measured at the time of initial examination were within reference limits. A CBC revealed leukopenia (3.2 × 10^3 WBCs/µL; reference range, 5.6 to 11.4 × 10^3 WBCs/µL) characterized by band neutrophilia (0.288 × 10^3 band neutrophils/µL; reference range, 0 to 0.1 × 10^3 band neutrophils/µL) and neutropenia (1.280 × 10^3 neutrophils/µL; reference range, 2.9 to 8.5 × 10^3 neutrophils/µL). Initial biochemical abnormalities included an anion gap of 15 mmol/L (reference range, 16 to 21 mmol/L), slightly high CO₂ content (30 mmol/L; reference range, 21 to 29 mmol/L), mild hypokalemia (2.8 mmol/L; reference range, 2.9 to 4.5 mmol/L), hyperglycemia (181 mg/dL; reference range, 64 to 132 mg/dL), and mild hyperaluminemia (3.5 g/dL; reference range, 2.2 to 3.4 g/dL). Results of other preanesthetic blood tests were unremarkable. Abdominocentesis yielded a yellow, cloudy fluid with a nucleated cell count of 2.5 × 10^3 nucleated cells/µL and protein concentration of 3.0 g/dL (reference range, <2.5 g/dL). The horse still had signs of pain after IV administration of 2 doses of xylazine (150 mg each). Therefore, a decision was made to perform an exploratory celiotomy.

Potassium penicillin (22,000 U/kg [10,000 U/lb], IV) and gentamicin (6.6 mg/kg [3 mg/lb], IV) were given 30 minutes prior to anesthetic induction. The horse was premedicated with xylazine (0.82 mg/kg [0.37 mg/lb], IV), and anesthesia was induced 4 minutes later with diazepam (0.05 mg/kg [0.023 mg/lb], IV) and ketamine (1.98 mg/kg [0.9 mg/lb], IV). The horse was blindly intubated with a 30-mm endotracheal tube, and the cuff was inflated to a pressure of 90 to 100 cm H₂O. A demand valve set to a rate of 10 breaths/min was used until the horse was hoisted onto the surgery table. An anesthetic machine equipped with a large animal circuit was attached to the endotracheal tube, and isoflurane (delivered concentration, 3%) in oxygen (10 L/min) was administered. The oxygen flow rate was decreased to 3 L/min after 10 minutes, when end-tidal isoflurane concentration, measured with a gas analyzer, was 1.2%. A 14-gauge catheter was inserted in a jugular vein, and a balanced electrolyte solution was administered at a rate of 10 mL/kg/h (4.5 mL/lb/h). A bolus of lidocaine (2.5 mg/kg [1.1 mg/lb], IV) was administered immediately after administration of isoflurane was begun, followed by a constant rate infusion of lidocaine (0.05 mg/kg/min). Administration of dobutamine (maximum, 2 µg/kg/min [0.9 µg/lb/min]) was initiated before direct blood pressure readings were obtained; the rate was adjusted as needed to maintain mean arterial pressure between 75 and 85 mm Hg. Body temperature was continuously monitored with an indwelling nasal probe and ranged from 37°C (98.6°F) at the beginning of surgery to 35°C (95°F) at the end of surgery. A forced-air warming system was placed over the sternum and neck of the horse and set to a temperature of 43°C (109.4°F). Electrocardiography and pulse oximetry were used to monitor the horse, and a sidestream gas analyzer was attached to the anesthetic circuit.

The initial heart rate was 41 beats/min and stayed in the range of 28 to 41 beats/min for the entire surgical period. The respiratory rate was controlled at 10 breaths/min by means of intermittent positive-pressure ventilation set to a tidal volume of 10 mL/kg and peak inspiratory pressure of 25 cm H₂O. A 20-gauge 1-inch catheter was placed in the transverse facial artery to allow direct monitoring of blood pressure. Initial systolic, diastolic, and mean blood pressures were 90, 66, and 70 mm Hg, respectively, but decreased to 78, 48, and 60 mm Hg 5 minutes later. One liter of hypertonic (7.2% NaCl) saline solution was administered at this time to increase arterial blood pressure, but the expected rapid response was not seen. Ephedrine (0.06 mg/kg [0.027 mg/lb], IV) was administered 20 minutes after gas anesthesia was begun to further increase blood pressure. After administration of ephedrine, systolic, diastolic, and mean blood pressures immediately increased to 140, 90, and 104 mm Hg, respectively. Flunixin meglumine (800 mg, IV) was given at this time, as it had not been given prior to anesthetic induction. An arterial blood sample was obtained 17 minutes after induction of anesthesia, and blood-gas analyses were performed with a portable analyzer (Table 1). The mean arterial pressure continued to be maintained. Ephedrine (0.05 mg/kg [0.023 mg/lb], IV) and ketamine (1.98 mg/kg [0.9 mg/lb], IV) were given at this time, as it had not been given prior to anesthetic induction. An arterial blood sample was obtained 17 minutes after induction of anesthesia, and blood-gas analyses were performed with a portable analyzer (Table 1). The mean arterial pressure continued to be maintained.
Table 1—Results of serial arterial blood gas analyses performed in a horse that developed acute pulmonary embolism while anesthetized.

<table>
<thead>
<tr>
<th>Variable</th>
<th>17</th>
<th>28</th>
<th>42</th>
<th>59</th>
<th>101</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.42</td>
<td>7.30</td>
<td>7.325</td>
<td>7.348</td>
<td>7.43</td>
<td>7.32 to 7.44</td>
</tr>
<tr>
<td>Paco₂ (mm Hg)</td>
<td>48.8</td>
<td>61.5</td>
<td>56.1</td>
<td>50.7</td>
<td>41.5</td>
<td>36 to 46</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>400</td>
<td>93</td>
<td>136</td>
<td>194</td>
<td>249</td>
<td>90 to 100</td>
</tr>
<tr>
<td>BE (mmol/L)</td>
<td>+7</td>
<td>+4</td>
<td>+3</td>
<td>+4</td>
<td>+3</td>
<td>−5 to +5</td>
</tr>
<tr>
<td>HCO₃⁻ (mmol/L)</td>
<td>31.7</td>
<td>30.4</td>
<td>29.5</td>
<td>29.2</td>
<td>28.1</td>
<td>24 to 30</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>n/a</td>
<td>1.02</td>
<td>n/a</td>
<td>n/a</td>
<td>1.19</td>
<td>0.3 to 1.5</td>
</tr>
<tr>
<td>iCa²⁺ (mmol/L)</td>
<td>1.33</td>
<td>n/a</td>
<td>1.28</td>
<td>1.25</td>
<td>n/a</td>
<td>1.25 to 1.75</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>100</td>
<td>96</td>
<td>96</td>
<td>100</td>
<td>100</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>PetCO₂ (mm Hg)</td>
<td>37</td>
<td>19</td>
<td>25</td>
<td>35</td>
<td>29</td>
<td>35 to 45</td>
</tr>
<tr>
<td>Dead space (%)</td>
<td>24</td>
<td>69</td>
<td>55</td>
<td>31</td>
<td>30</td>
<td>&lt; 50</td>
</tr>
</tbody>
</table>

Paco₂ = Arterial partial pressure of CO₂, PaO₂ = Arterial partial pressure of O₂, BE = Base excess, HCO₃⁻ = Bicarbonate, iCa²⁺ = Ionized calcium, SaO₂ = Saturation of hemoglobin with oxygen, PetCO₂ = End-tidal partial pressure of CO₂.

Dead space was calculated as the ratio of physiologic dead space to tidal volume by use of the following equation: dead space = (Paco₂ − PetCO₂) / Paco₂.

...used to increase; therefore, butorphanol (0.02 mg/kg, IV) was given 20 minutes after induction of anesthesia to control pain and ensure an adequate level of anesthesia, as the surgeons were about to make the initial skin incision. End-tidal isoflurane concentration at this time was 1.1%.

Approximately 22 minutes after administration of isoflurane was begun, a sharp decrease in end-tidal partial pressure of CO₂ (PetCO₂) was observed. The PetCO₂ had initially been 34 to 37 mm Hg but suddenly decreased to 19 mm Hg. The PetCO₂ continued to decrease until it reached a nadir of 16 mm Hg within 2 minutes after the initial sharp decrease was observed.

**Question**

What are the possible causes for the sudden decrease in PetCO₂ in this patient?

**Answer**

Possible causes for the decrease in PetCO₂ in this patient include severe cardiovascular disturbance (cardiac arrest), hyperventilation, hypothermia, vasoconstriction, ventilator failure, airway leak or disconnection, pulmonary embolism, and capnograph malfunction. ¹

Mean arterial pressure was > 100 mm Hg, ruling out cardiac arrest. In an attempt to correct any hyperventilation that may have been present, the peak inspiratory pressure was decreased to 20 cm H₂O and the respiratory rate was decreased to 8 breaths/min. However, this had no apparent effect on PetCO₂, ruling out hyperventilation as the cause of the sudden decrease. Hypothermia was also ruled out because the patient's body temperature was 36.6°C (97.8°F). Vasoconstriction was considered a possibility because of the administration of ephedrine, but ephedrine typically does not cause the type of severe central vasoconstriction that would lead to these results. Also, there was not a direct temporal relationship between administration of ephedrine and the decrease in PetCO₂. The ventilator was working properly, and no other equipment malfunctions were identified. In addition, no abnormalities consistent with an equipment malfunction were seen when another horse was anesthetized with the same anesthesia machine and gas analyzer later that same day, suggesting that the sudden decrease in PetCO₂ was not a result of an equipment malfunction.

Serial arterial blood samples were obtained and submitted for blood gas analysis after the decrease in PetCO₂ was noticed. There were substantial differences between results obtained prior to the decrease in PetCO₂ and results obtained for follow-up samples (Table 1). In addition, the mucous membranes had developed a dark pink color that was not present earlier.

Over the next 30 minutes, the PetCO₂ began to rise steadily, increasing from 21 to 36 mm Hg. However, the mucous membranes remained dark pink for the remainder of the surgical procedure. Given the high calculated dead space percentage, rapidity of onset of the decrease in PetCO₂, lack of evidence for other potential causes, and slow resolution of the abnormality, pulmonary embolism was suspected to be the cause of the sudden decrease in PetCO₂. The remainder of the anesthetic period and the recovery period were unremarkable.

**Discussion**

There are a number of types of pulmonary emboli, including air, fat, thrombi, polymethyl methacrylate, tumors, septic masses, hydatid cysts, amniotic fluid, and foreign bodies. ¹ A fat embolus can be ruled out as the cause of the sudden decrease in PetCO₂ in the horse described in the present report because surgery had not yet begun at the time clinical signs were identified. Similarly, a polymethyl methacrylate embolus can be ruled out because this product was not used in this patient. A thrombus was unlikely because results of a clotting profile (prothrombin time, partial thromboplastin time, and thromboelastography) performed 55 minutes after the sudden decrease in PetCO₂ were normal. An amniotic fluid embolus can be ruled out because the horse was not pregnant. A neoplastic or hydatid embolus was possible but would have required computed tomography or necropsy for confirmation, and septic emboli were possible given the patient's condition. However, in people, septic embolism typically causes nonspecific
signs that develop over a long period, rather than acute signs, as was the case for the horse described in the present report.

Venous air embolism in dogs, cats, and horses undergoing various procedures has been reported previously. Some of these procedures included administration of air, such as for negative-contrast radiography or insufflation for endoscopic procedures, and up to 23% of human patients undergoing hand-injected, contrast-enhanced computed tomography reportedly have non-fatal venous air embolism. In patients who are awake, symptoms of air embolism can include acute dyspnea, persistent cough, lower respiratory tract sounds (such as wheezing and rales), and tachypnea. Changes that have also been described include electrocardiographic abnormalities, development of a murmur, hypotension, pulmonary edema, neurologic deficits, pruritus, and death. In anesthetized patients, the most common clinical abnormalities are decreases in PETCO2, oxygen saturation (SaO2), and arterial partial pressure of oxygen (PaO2). The embolus prevents pulmonary arterial blood from flowing to part of the lung, which prevents gas exchange in those alveoli, resulting in an increase in physiologic dead space. The CO2 from the pulmonary blood cannot diffuse into the alveoli, with the result that these alveoli do not contain any CO2. During exhalation, the gas from these alveoli, which does not contain any CO2, mixes with gas from the alveoli that are still participating in gas exchange, diluting the CO2 in the expired gas and resulting in the low PETCO2 value. However, arterial partial pressure of CO2 (PaCO2) is typically high, because of an increase in physiologic dead space resulting from severe ventilation-perfusion mismatch.

Fundamentally, a high PaCO2 is a result of a decrease in ventilation relative to the production of CO2. This can be due to a marked increase in production of CO2, such as occurs with hyperthermia, or a decrease in alveolar ventilation, such as occurs with hypoventilation. Hypoventilation can be caused by severe ventilation-perfusion mismatch, drugs, muscle weakness, and obesity. The horse described in the present report was being mechanically ventilated, ruling out muscular weakness, obesity, and drugs as possible causes of hypoventilation leading to high PaCO2. There was no evidence of hyperthermia or other conditions associated with an increase in metabolism, as body temperature, heart rate, and other indices remained steady. Hence, in this patient, the high PaCO2 was most likely a result of a ventilation-perfusion mismatch.

The horse described in the present report had several signs that led us to conclude it had an embolism. The most prominent of these was the acute but transient decrease in PETCO2. Other signs included the increase in PaCO2, the severe decreases in PaO2 and SaO2, and the increased percentage in dead space. The transient nature of the clinical signs would not be consistent with a fat embolus or thrombus but because air dissipates over time, would be consistent with an air embolus.

It has been documented that the most important factors associated with death in dogs with experimentally induced venous air embolism are the amount of air entering the veins, the speed of entry, and the position of the body when air embolization occurs. In dogs, the lethal dose of air is approximately 7.5 to 15 mL/kg (3.4 to 6.8 mL/lb), whereas in rabbits, the lethal dose is 0.5 to 0.75 mL/kg (0.23 to 0.34 mL/lb). However, in critically ill patients in which hemodynamics are compromised, the lethal dose may be much smaller. Given that the horse described in the present report was being anesthetized for colic surgery and was dehydrated, it is possible that a relatively low volume of air could have caused the clinical signs that were observed. We calculate that the maximum amount of air contained in the IV fluid administration set that was used was only 60 mL. However, air could have been introduced by other means, such as a loose catheter cap or during administration of drugs.

Postoperatively, horses with pulmonary embolism can have neurologic sequelae that can manifest as changes in mental status or vision or as vestibular disease, and a previous report of a horse with pulmonary embolism indicated that the horse developed pruritus after recovering from anesthesia. The horse described in the present report developed neurologic abnormalities 18 hours after recovering from anesthesia, at which time it was treated for cerebral edema. Six weeks after discharge, the patient had a normal neurologic status. The patient returned to the Veterinary Teaching Hospital for treatment of colic approximately 60 days after the initial surgery, but was otherwise normal. Treatment consisted of IV administration of fluids and analgesics and a gradual reintroduction of feed, and the horse was discharged.

Early detection of venous air embolism is crucial for successful treatment. Monitoring PETCO2 and calculating physiologic dead space may help in the diagnosis of acute pulmonary embolism. End-tidal partial pressure of CO2 is typically an accurate indicator of PaCO2 in horses, but substantial differences can be seen in horses placed in dorsal recumbency and in horses with colic. For horses that are suspected to have venous air embolism while anesthetized, treatment should include occluding any portal of entry for air, instituting intermittent positive-pressure ventilation to increase intrathoracic pressure, administering fluids IV to increase central venous pressure, increasing the inspired oxygen percentage (if 100% oxygen is not being used), and discontinuing administration of nitrous oxide if it is being used because nitrous oxide will increase the size of venous air bubbles. Methods to support cardiovascular function may include administration of positive inotropes, such as dobutamine or dopamine. In the horse described in the present report, pulmonary embolism was suspected on the basis of the sudden decrease in PETCO2, increase in PaCO2, and decrease in PaO2 and by ruling out other possible causes. No long-term adverse sequelae were identified. Careful monitoring of anesthetized horses will enable the prepared anesthetist to properly diagnose and manage unusual events such as documented in this report.

c. Bair Hugger, Augustine Medical, Wakefield, UK.
d. i-Stat, Heska, Waukesha, Wis.
e. Willoughby tubing, Jorgensen Labs Inc, Loveland, Colo.
References

8. Martin L. All you really need to know to interpret arterial blood gases. 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 1999;27–29.