Anesthesia Case of the Month

In cooperation with the American College of Veterinary Anesthesiologists

History

A 4-year-old 74-g (0.034-lb) male sun conure (*Aratinga solstitialis*) was referred to the University of Georgia Veterinary Teaching Hospital for evaluation of a keel lesion. One month earlier, the owner had found the bird injured and bleeding in its cage. The referring veterinarian had cleaned the wounds and begun treatment with amoxicillin-clavulanic acid (95 mg/kg [43 mg/lb], PO, q 12 h). The wounds healed, but 2 weeks later, the bird began to pick at the area.

After an initial physical examination was performed at the teaching hospital, the bird was anesthetized with isoflurane delivered by mask and radiography was performed. On radiographs of the thorax, a large sequestrum of the keel was seen. The bird recovered from anesthesia without difficulties. Results of a CBC and serum biochemical profile were within reference limits.

The next day, the bird was premedicated with butorphanol (1.0 mg/kg [0.45 mg/lb], IM), and 25 minutes later, anesthesia was induced with isoflurane delivered by mask. The patient was intubated with moderate difficulty with a flexible Cook catheter,[a] and anesthesia was maintained with isoflurane in oxygen. An intraosseous catheter was then placed in the left ulna, and administration of 2.5% dextrose in half-strength lactated Ringer's solution was begun at a rate of 10 mL/kg/h (4.5 mL/lb/h). The surgery site was prepared with chlorhexidine and water, and the patient was transferred to the operating room.

In the operating room, a Doppler ultrasonic flow detector was placed for measurement of pulse rate. **End-tidal partial pressure of CO_2 ($P_{ET}CO_2$)** was monitored with an in-stream analyzer,[b] and cloacal temperature was monitored with a temperature probe. **Intermittent positive-pressure ventilation (IPPV)** was started with a pressure-cycled ventilator[c] at a rate of 8 breaths/min and **peak inspiratory pressure (PIP)** of 0.8 cm H_2O. Thoracic excursions were monitored visually to confirm appropriate tidal volume delivery. A circulating warm-water pad was placed under the bird, and a forced-air warming system[d] was started to deliver 43°C (109.4°F) air around the patient. The isoflurane vaporizer was set to 2.5%, and oxygen flow was set to 1 L/min at the start of surgery. The bird's cloacal temperature at the time of transfer to the operating room was 35.5°C (95.9°F).

Ten minutes after the bird was moved to the operating room, $P_{ET}CO_2$ increased from 35 to 50 mm Hg, and heart rate increased from 335 to 360 beats/min. The IPPV rate was increased to 14 breaths/min, and PIP was increased to 1.5 cm H_2O. Despite these measures, $P_{ET}CO_2$ did not change for the next 10 minutes. At this time, surgery was begun. During the 20 minutes the patient had been in the operating room, the cloacal temperature had steadily increased. Five minutes after surgery was begun, the heart rate was > 380 beats/min and $P_{ET}CO_2$ had increased to 78 mm Hg. The vaporizer setting was increased to 2.75%, and the IPPV rate was increased to 16 breaths/min. At this time, cloacal temperature was 42.8°C (109°F), so the forced-air warming system was set to deliver air at 35°C (95°F). Two minutes later, the cloacal temperature had increased to 43.9°C (111.0°F). The forced-air warming system and circulating warm-water blanket were turned off.

Two minutes later, cloacal temperature had increased further to 47.2°C (117.0°F). At this time, administration of isoflurane was discontinued, and administration of propofol as a continuous rate infusion was begun at a rate of 0.4 mg/kg/min (0.18 mg/lb/min). A bolus of 5 mL of 2.5% dextrose in half-strength lactated Ringer's solution was given. The $P_{ET}CO_2$ continued to increase until it reached 97 mm Hg, after which it decreased abruptly to 8 mm Hg, and a pulse could no longer be detected with the Doppler ultrasonic flow detector.

Cardiac arrest was diagnosed at this point. The propofol infusion was discontinued; epinephrine (0.027 mg/kg [0.012 mg/lb]) and atropine (0.033 mg/kg [0.015 mg/lb]) were given via the intraosseous catheter, and external cardiac massage was begun. One minute later, additional doses of epinephrine and atropine were given. The $P_{ET}CO_2$ then decreased to 0 mm Hg, and resuscitative efforts were discontinued.

The patient's temperature was recorded with 3 thermometers, each of which reported a final temperature of 48.1°C (118.6°F). Results of analysis of an intracardiac blood sample obtained shortly after death were as follows: pH, 6.89 (reference range, 7.4 to 7.45); P_{CO_2}, 100.8 mm Hg (reference range, 35 to 45 mm Hg); P_{O_2}, 73 mm Hg (reference range depends on collection site); HCO_3 concentration, 18 mEq/L (reference range, 22 to 24 mEq/L); base excess, –14 mEq/L (reference range, 0 to –5 mEq/L); glucose concentration, 222 mg/dL (reference range, 200 to 345 mg/dL); and potassium concentration, > 9.0 mmol/L (reference range, 3.4 to 5.0 mmol/L).

Question

What are the possible causes of fatal hyperthermia in this patient?

Answer

Possible causes of hyperthermia include malignant hyperthermia, thyrotoxicosis, tremors, pheochromocytoma, administration of certain drugs, hypothalamic dysfunction, and decreased heat loss (ie, heat stroke).[1]

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Our initial suspicion was that the ambient warming techniques we had used (ie, the forced-air warming system and the circulating warm-water pad) had induced heat stroke. It has been our experience that small animals with a high surface area-to-weight ratio tend to have rapid increases in body temperature with external warming measures. However, discontinuing these external warming efforts had no impact on the increase in cloacal temperature in this patient. Also, if the increase in cloacal temperature had been a result of the ambient warming techniques, then we would have expected that cloacal temperature would not have exceeded the highest setting on the forced-air warming system (43°C [109.4°F]). Terminally, however, the patient's temperature clearly exceeded this value.

At necropsy, diffuse moderate chronic left ventricular hypertrophy, mild multifocal acute degeneration and contraction band necrosis of the biceps femoris muscle, and diffuse moderate acute congestion of the lungs were documented. Left ventricular hypertrophy may have contributed to the sudden death in this case but would not be expected to be responsible for the hyperthermia or hypercarbia.

Once the hypercarbia was identified in this bird, there was concern that it had a hypermetabolic condition resulting in overproduction of CO_2,[2] such as malignant hyperthermia, sepsis, or thyrotoxicosis. Malignant hyperthermia can be triggered by inhalant anesthetics and is frequently (70%) fatal without rapid treatment with dantrolene, a calcium channel blocker.[3] We discontinued administration of isoflurane in this patient on the supposition that the hyperthermia and hypercarbia may have been a result of a malignant hyperthermia event. However, to our knowledge, malignant hyperthermia per se has not been reported in any avian species, although turkeys do have a phenomenon that is similar to malignant hyperthermia.[4] In addition, postmortem examination in this patient did not reveal any of the lesions typically induced by malignant hyperthermia.

Sepsis was unlikely to have been the cause of the hyperthermia and hypercarbia in this patient in that its condition was stable prior to surgery, results of preoperative clinicopathologic testing were within reference ranges, and no septic nidus was found on postmortem examination. Thyrotoxicosis was a possible consideration but considered unlikely because thyroid tissue was not found to be abnormal on postmortem examination.

Discussion

Tachycardia in this patient may have been a result of the increase in core body temperature or the hypercarbia. Humans undergoing whole-body warming have marked increases in heart rate,[5] and hypercarbia is a not-infrequent cause of sympathetic stimulation in animals.[6] The mixed respiratory-metabolic acidosis seen after death was consistent with overproduction of CO_2 or profound hypoventilation as well as with release of organic acids, most likely as a result of cell death secondary to the high temperature.[6] Hyperkalemia is an inconsistent finding in other species with hyperthermia but may have indicated severe tissue destruction in this patient.[7]

Measuring P_{ETCO_2} during IPPV is a useful method of monitoring for rapid increases in whole-body metabolism. In dogs with hyperthermia, increases in P_{ETCO_2} precede changes in rectal temperature by 2 to 4 minutes.[8,9] In spontaneously breathing animals, changes in respiratory rate or depth may compensate for these increases in P_{ETCO_2} and mask abrupt changes in P_{ETCO_2} that are attributable to hypermetabolism. In the bird described in the present report, because of the IPPV, the change in P_{ETCO_2} occurred concurrent with the increase in heart rate.

Airway pressures used in this patient were significantly lower than those typically used in dogs and cats. The ventilator used in this bird was a pressure-cycled ventilator that 1 author has used for 4 years and the other has used for 10 years. In that time, we have observed that relatively low PIPs (< 5 cm H_2O) are required for adequate ventilation in birds, as assessed by visual inspection of thoracic excursions and monitoring of P_{ETCO_2}. In a previous study,[10] airway pressures of 5 cm H_2O were used in African grey parrots weighing 250 g. In the patient described in the present report, as in all our avian patients, we observed thoracic excursions after making the initial settings to confirm that they were adequate. In-stream monitoring of P_{ETCO_2} was used to ensure adequate ventilation, and monitoring P_{ETCO_2} has been documented to produce results similar to those associated with monitoring arterial partial pressure of CO_2 in chickens[11] and African grey parrots[10] during IPPV. On the basis of these observations, we believe that ventilation was adequate up until the time when a hypermetabolic event occurred and CO_2 production exceeded CO_2 elimination. Another important piece of information to consider is the bird's weight of 74 g. In our experience, birds this small require quite low levels of PIP to maintain adequate ventilation, as determined by observing thoracic excursions and monitoring P_{ETCO_2}. Finally, if the hypercarbia in this patient had been a result of inappropriate ventilator settings, we would have expected the P_{ETCO_2} to have increased slowly rather than abruptly. On the other hand, inappropriate ventilator settings may have compounded the hypercarbia caused by a hypermetabolic state.

Several weeks after this event, a second small patient in the same operating room experienced hyperthermia of unknown cause, which was treated successfully. At this time, the operating room lamps were investigated, and 1 lamp was found to be capable of producing a temperature of 48.9°C (120°F) at the table surface. The bulb was changed in this lamp, but the lamp continued to produce this excessive temperature. Because we were unable to determine any other cause for the fatal hyperthermia in the bird described in the present report, we suspect that the heat generated by the operating room lamp caused heat stroke, resulting in hyperthermia.

Technical and mechanical failures continue to be an important component of anesthetic complications and death in human medicine.[12] Although most technical failures relate to the anesthesia machine, other devices used in the management of anesthesia should not be ignored. Devices that are known to be functioning incorrectly should be replaced or not used to avoid a catastrophic outcome.

a. Global Veterinary Products Inc, New Buffalo, Mich.
b. ET_{CO_2}/Sp_{O_2} monitor, Novametrix Medical Systems Inc, Wallingford, Conn.
c. Vetronics ventilator, Bioanalytical Systems Inc, West Lafayette, Ind.
d. Bair Hugger, Augustine Medical, Wakefield, UK.

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