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Anesthesia Case of the Month

History

A 13-year-old 8.7-kg (19.1-lb) castrated male mixed-breed dog was referred to the Neurology Service of the University of Minnesota Veterinary Medical Center for evaluation after being examined by the referring veterinarian 5 days prior. At the time of the referring veterinarian visit, the dog had a 2-day history of once-daily fainting episodes when excited, a left-sided head tilt, lethargy, incoordination, inappetence, restlessness, and exophthalmos of the right eye. Other pertinent history included recent rough play with a larger dog, occasional coughing and sneezing, and mild intermittent bradycardia (58 to 80 beats/min) as diagnosed by the referring veterinarian. Additionally, protein-losing nephropathy had been diagnosed 9 months previously as well as recurrent urinary tract infections, and the patient was currently receiving enalapril (0.57 mg/kg [0.26 mg/lb], PO, q 24 h) and aspirin (0.52 mg/kg [0.24 mg/lb], PO, q 24 h).

A CBC, serum biochemical analysis, and urinalysis had been performed by the referring veterinarian 5 days prior to referral and revealed azotemia (BUN concentration, 27 mg/dL [reference range, 7 to 25 mg/dL]; creatinine concentration, 2 mg/dL [reference range, 0 to 1.4 mg/dL]), hyposthenuria (urine specific gravity, 1.011; reference range, 1.016 to 1.060),[1] a high urine protein-to-creatinine ratio (3.3; reference range, < 0.5 to 1), hyponatremia (132 mmol/L; reference range, 138 to 160 mmol/L), and slightly high serum alkaline phosphatase activity (166 U/L; reference range, 20 to 150 U/L).

Physical examination revealed swelling, heat, and signs of discomfort of the right eye, and mild clinical evidence of dehydration. Examination of the left ear revealed no abnormalities, but a painful response prevented examination of the right ear. A slight increase in bronchovesicular sounds was noted in all quadrants during thoracic auscultation, which was attributed to referred stridor from the left nostril, where decreased airflow was noted but no gross anatomic abnormalities were found.

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Further diagnostic evaluation under general anesthesia was planned, including examination of the right ear, an oral examination by the dentistry service with or without full dental radiographs, and CT of the head and cervical spine. The patient was premedicated with hydromorphone hydrochloride (0.1 mg/kg [0.045 mg/lb], IM) and midazolam (0.1 mg/kg, IM), and a 20-gauge IV catheter was placed in the right cephalic vein. Prior to induction of general anesthesia, the patient was preoxygenated by means of administration of oxygen at a flow rate of 4 L/min for 5 minutes via a face mask attached to a Bain modification of a Mapleson D nonrebreathing circuit. Anesthesia was then induced with propofol (2.5 mg/kg [1.1 mg/lb], IV, to effect; total dose, 22 mg) and orotracheally intubated with an 8-mm (internal diameter) endotracheal tube. General anesthesia was maintained with isoflurane (2% to 2.5%) in oxygen. A 1-L bag of lactated Ringer solution with a 60 drops/mL administration set was attached to the IV catheter, but IV fluid administration did not immediately commence because of anticipated transport of the patient to the CT suite.

For the dental and aural examinations, the patient was positioned first in sternal recumbency, then in right lateral recumbency and was allowed to breathe spontaneously. Blood pressure and heart rate were measured with an ultrasonographic Doppler device and a sphygmomanometer with a size 3 cuff placed proximal to the tarsal region of the right hind limb. The oxygen saturation of hemoglobin as measured by pulse oximetry (Spo_2) was monitored with a portable pulse oximeter, and respiratory rate was monitored by observing movement of the reservoir bag. All measured parameters were within reference limits throughout, and no complications were noted during the oral and aural examinations, which took approximately 15 minutes. At the conclusion of the oral and aural examinations, immediately prior to movement of the patient to a gurney for transport, the patient's condition was stable (systolic arterial blood pressure, 110 mm Hg; heart rate, 78 beats/min; respiratory rate, 10 beats/min; Spo_2, 100%). However, on repositioning of the patient in left lateral recumbency on the gurney, there was immediate evidence of acute oxygen desaturation (Spo_2 of 78% despite inhaled oxygen concentration > 95%). The heart rate was 75 beats/min as measured with the pulse oximeter and palpation of a femoral artery. Systolic blood pressure, measured indirectly, was 110 mm Hg. Respiratory rate, determined by direct observation of thoracic wall excursions, was 10 breaths/min. The plane of anesthesia was determined to be appropriate, as indicated by loose jaw tone and ventromedial eye position with no palpebral reflex

present. The isoflurane vaporizer setting was 2% (1.5X minimum alveolar concentration). Appropriate placement of the endotracheal tube in the trachea was confirmed via direct examination with a laryngoscope, bilateral thoracic auscultation, and palpation of the tip of the endotracheal tube proximal to the thoracic inlet. Manual intermittent positive-pressure ventilation (IPPV) was instituted to a peak inspiratory pressure of 20 cm H_2O; no resistance to manual ventilation was noted. After approximately 1 minute of IPPV, Spo_2 was 100%. A portable capnograph monitor was then attached between the machine end of the endotracheal tube and the breathing circuit to allow continuous monitoring of end-tidal partial pressure of carbon dioxide ($Petco_2$); $Petco_2$ was initially noted to be 30 mm Hg.

The patient was transferred to the CT suite in left lateral recumbency, with manual positive pressure ventilation provided during transport (duration of transport, 10 minutes). During the transfer, the pulse oximeter showed evidence of rapid oxygen desaturation (Spo_2, 80%), and the $Petco_2$ decreased to 27 mm Hg. The patient's heart rate was 83 beats/min; systolic blood pressure was 55 mm Hg. The isoflurane vaporizer setting was therefore decreased from 2.5% to 1% to address the hypotension and hypoventilation. Consistent manual IPPV to a peak inspiratory pressure of 25 cm H_2O was instituted but did not improve the patient's Spo_2. An increased resistance to manual IPPV was noted and was attributed to a decrease in respiratory system compliance. Albuterol (0.01 mg/kg [0.0045 mg/lb]; total dose, 90 µg) was administered via the endotracheal tube. The patient's Spo_2 improved to 90%. No arterial blood gas analysis was performed. In the absence of partial pressure of oxygen in arterial blood (Pao_2) data, a presumptive diagnosis of hypoxemia was made on the basis of evidence of hemoglobin desaturation represented by the low Spo_2. The patient was repositioned to sternal recumbency and continued to receive IPPV. Within several minutes, the Spo_2 was 100%, systolic arterial blood pressure was 90 mm Hg, diastolic arterial blood pressure was 42 mm Hg, mean arterial pressure was 60 mm Hg, and heart rate was 100 beats/min. Controlled ventilation continued at a respiratory rate of 10 breaths/min. With the patient in the CT suite and positioned for imaging, IV fluid therapy was initiated at a rate of 6.9 mL/kg/h (3.1 mL/lb/h).

During CT, the patient was positioned in sternal recumbency for imaging of the cervical spine, head, and thorax. The patient was mechanically ventilated to a tidal volume of 180 mL (20.7 mL/kg [9.4 mL/lb]) and peak inspiratory pressure of 18 cm H_2O. Nine milliliters (1.03 mL/kg [0.47 mL/lb], IV) of an ioversol contrast agent was administered, with no change in blood pressure or heart rate noted. The Spo_2 was between 99% and 100% for the duration of the procedure. Mild hypotension (mean arterial pressure, 55 mm Hg), which occurred 5 minutes after the start of CT, immediately following administration of the contrast agent, was treated with a decrease in the vaporizer setting from 1.5% to 1.25% and administration of an IV fluid bolus (5 mL/kg [2.3 mL/lb]). Fluid therapy then resumed at a rate of 6.9 mL/kg/h, IV, and the systolic and mean arterial pressure values increased to 90 mm Hg and 55 to 60 mm Hg, respectively. At the conclusion of CT (total duration, 15 minutes), the patient was transported back to the recovery area. On arrival, mean arterial blood pressure was 60 mm Hg, and $Petco_2$ was 40 mm Hg; no other parameters were recorded, and shortly thereafter, anesthesia was discontinued. The patient was positioned in sternal recumbency with close monitoring of respiration, Spo_2, blood pressure, and $Petco_2$. The patient recovered from general anesthesia without apparent complications.

Computed tomography revealed multiple areas of intraluminal mineralization of the fifth- or sixth-order branches of the right caudal lobar pulmonary artery. Several of the branches lacked contrast filling distally. Mild atelectasis was noted in the right ventral lung lobes. When the right and left orbital regions were compared, attenuation of one of the arterial branches was evident in the right orbital region, with overall decreased blood flow to that side. These findings suggested multiple acute (soft tissue) and chronic (mineralized) pulmonary thromboemboli and a right retrobulbar thrombus causing the orbital swelling **(Figure 1)**.

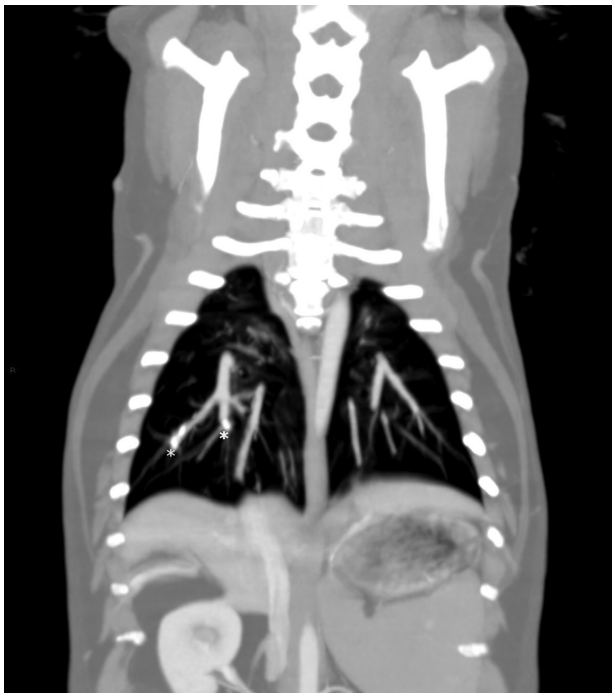

Figure 1—Maximum-intensity dorsal multiplanar reformatted CT image (window width, 1,600 Hounsfield units; window level, 550 Hounsfield units) of the thorax of a 13-year-old castrated male mixed-breed dog with an acute onset of syncope when excited and neurologic signs (left-sided head tilt, lethargy, and incoordination). Multiple areas of intraluminal mineralization of the right caudal lobar pulmonary artery (asterisk) are evident, consistent with a diagnosis of chronic pulmonary thromboemboli. Contrast attenuation consistent with acute pulmonary thromboemboli and mild atelectasis of the right ventral lung lobes is also evident.

Question

Which of the 5 causes of hypoxemia is the most likely reason for the rapid oxygen desaturation (as represented by the acute decrease in Spo_2) that occurred during general anesthesia in this patient?

Answer

There are 5 causes of hypoxemia[2,3]: hypoventilation, low inspired oxygen fraction, anatomic shunt, diffusion impairment, and ventilation-perfusion mismatch. On the basis of results of CT, the primary differential diagnosis for this patient's acute oxygen desaturation was ventilation-perfusion mismatch, which can be subclassified into venous admixture versus dead-space ventilation (wasted ventilation). In the patient of the present report, we suspected that the combination of chronic thromboemboli causing obstruction of the pulmonary vasculature and atelectasis (as a result of general anesthesia and positioning) affected a sufficiently large portion of the lungs to result in the clinical signs observed. The combination of atelectasis and the thromboemboli noted on CT would cause mixed ventilation-perfusion mismatch, with aspects of both dead-space (ie, wasted) ventilation and venous admixture. Results of CT suggested the presence of both acute and chronic thromboemboli within the pulmonary vasculature. Such pulmonary thromboemboli obstruct numerous pulmonary blood vessels in affected patients, preventing perfusion of multiple alveoli. Without alveolar perfusion, blood cannot be delivered to participate in gas exchange; however, the involved alveoli are still being ventilated normally. In affected patients, atelectasis results in alveolar collapse such that these alveoli do not participate in gas exchange, but many may have continued to be perfused. As such, pulmonary gas exchange is compromised in both of these scenarios. When a large enough area of the lungs is affected, oxygen exchange may be compromised, resulting in hypoxemia.[4–6]

In the patient of this report, we suggest that the chronic thromboemboli did not affect gas exchange severely in the absence of atelectasis, when the patient was conscious. However, during general anesthesia, sufficient lung parenchyma was compromised by atelectasis and, in combination with a decreased ventilatory drive, hypoxemia resulted. Subclinical thromboemboli have been described in human patients, with identification occurring only at autopsy.[7,8] Pulmonary thromboemboli prevent perfusion of alveoli that are still being ventilated, and this prevents blood from reaching the alveoli to participate in gas exchange. For the patient described in the present report, CT results indicated that the right-sided pulmonary parenchyma was more severely affected than the left-sided pulmonary parenchyma. When the patient was placed in left lateral recumbency, the dependent left-sided parenchyma could not fully expand to compensate for the right-sided disease.[9] Because this patient's disease apparently resulted from compromised perfusion to a greater extent than ventilation mismatch, it was nonresponsive to an increased inspired oxygen concentration or to administration of a bronchodilator (albuterol). Effective treatment consisted of repositioning the patient to sternal recumbency, which likely enabled regions of the lung that were being perfused more effectively to participate in gas exchange.

We suggest that the thromboembolic disease evident in the lung parenchyma and the right retrobulbar region of this patient was likely a complication of preexisting protein-losing nephropathy, which had been diagnosed in this dog 9 months previously. Thrombosis has been reported in 13% of dogs with glomerular disease.[10] Hypercoagulability in patients with protein-losing glomerular disease occurs because of a deficiency in antithrombin III.

Discussion

In the patient of the present report, which experienced rapid oxygen desaturation after positioning in lateral recumbency during general anesthesia, results of CT suggested the presence of both acute and chronic pulmonary thromboemboli; it is likely that atelectasis also contributed.

Ventilation-perfusion mismatch is a common cause of hypoxemia in anesthetized veterinary patients. The diagnosis is typically made by means of elimination. Ventilation-perfusion mismatch can affect an area of the lungs or can be diffuse and affect multiple regions or units of the pulmonary parenchyma. Hypoxemia is most frequently evident when multiple areas of the lung parenchyma are affected.

The patient of the present report initially improved with IPPV. Therefore, we concluded that the combination of pulmonary thromboemboli and atelectasis was the likely cause of the desaturation that was observed. Both absorption atelectasis (as can occur when the patient receives > 95% inspired oxygen) and positional atelectasis worsen with increased duration of general anesthesia.[11] We suspect the initial improvement in response to IPPV for our patient may have been the result of early, less severe atelectasis that subsequently worsened during transport to the CT suite. With increased duration (on arrival in the CT suite), IPPV could no longer sufficiently compensate for the atelectasis. Once the patient was repositioned in sternal recumbency, the positional atelectasis improved, and IPPV likely recruited areas of the lung unaffected by thromboemboli.

Orthostatic hypotension occurs in conscious humans, and it is also observed during general anesthesia.[12,13] During inhalant anesthesia, there is a blunting of baroreflex responses. Thus, when a patient is repositioned, a period of hypotension may occur until

the autonomic nervous system becomes active, resulting in an increase in cardiac output and vasoconstriction.[13–15] We observed hypotension in our patient shortly after movement and repositioning. In human patients under general anesthesia, the usual response to compensate for positional hypotension (ie, increased heart rate and vasoconstriction) is impeded.[15]

Management of the patient of the present report may have been improved with earlier initiation of IV fluid therapy. The dog had a history of inappetence and renal insufficiency and clinical evidence of dehydration on physical examination. Additionally, because of the possible history of recent head trauma in this patient, ideal monitoring would have included capnography and frequent measurement of arterial blood gases from the beginning of general anesthesia. As the partial pressure of carbon dioxide in arterial blood ($Paco_2$) increases, vasodilation occurs, and in patients with head trauma, the ability of the brain to autoregulate in response to changes in $Paco_2$ is impaired. Hypoventilation can lead to increased intracranial pressure, whereas hyperventilation can lead to ischemia.[16] The availability of arterial blood gas data in this patient would have allowed us to compare the $Paco_2$ with the $Petco_2$. The difference between these 2 values should not exceed 5 mm Hg; however, in cases of ventilation-perfusion mismatch, there may be a large gradient between the $Paco_2$ and the $Petco_2$, with the $Petco_2$ lower than the reference range and the $Paco_2$ higher than the reference range. The difference between the $Paco_2$ and $Petco_2$ can be used to calculate wasted (dead-space) ventilation.[17] In a clinically normal conscious dog, the ratio of dead-space ventilation (anatomic and alveolar) to tidal volume is 35%, but this can reportedly[18] increase to 50% in small animal patients during general anesthesia. Further, in patients with pulmonary thromboemboli, there is an increase in wasted ventilation.[19] Had we been monitoring $Paco_2$ and $Petco_2$ throughout in the patient of this report, we would have expected a marked gradient, and this information may have helped us in reaching a definitive diagnosis sooner and instituting appropriate treatment more rapidly.

Monitoring of arterial blood gases in the patient of the present report would have also allowed us to compare the Pao_2 with the fraction of inspired oxygen. A pulse oximeter measures hemoglobin saturation, not the partial pressure of oxygen in the blood. For a clinically normal animal or human breathing room air (21% oxygen concentration), the pulse oximeter should read between 95% and 100%. Because the maximum pulse oximeter reading is 100%, the patient is provided with > 95% inspired oxygen when under general anesthesia; however, it is possible that a patient's hemoglobin saturation could be adequate (ie, 99% to 100%) even when pulmonary gas exchange is inadequate. It would not be possible to detect low Pao_2 in a patient receiving > 95% inspired oxygen without directly evaluating blood gas values.[20]

Hypoventilation is a common cause of hypoxemia in veterinary patients that are breathing room air (21% oxygen). However, anesthetized patients receive a higher percentage of inspired oxygen, such that hypoxemia as a result of hypoventilation is much less common. Hypoventilation and desaturation may be observed pre- or postoperatively as a result of analgesic or sedative drug administration and when supplemental oxygen administration has been discontinued. In general, the appropriate treatment for hypoventilation is oxygen supplementation, reversal or discontinuation of drugs that could be contributing (eg, opioids or inhaled anesthetics), and intubation with assisted ventilation if necessary.

It is possible for hypoxemia to develop in patients under general anesthesia as a result of delivery of an inappropriately low inspired oxygen concentration. Therefore, whenever a patient has evidence of desaturation, it is imperative to determine whether the oxygen supply is depleted or not turned on and to thoroughly troubleshoot the breathing circuit (eg, check whether hoses are kinked or disconnected and ensure the correct breathing circuit is connected to the fresh gas outlet). Furthermore, if a high (ie, > 30% oxygen) percentage of mixed medical-grade air or nitrous oxide is administered, the percentage of oxygen delivered to the patient will decrease. Again, the fraction of inspired oxygen available for gas exchange is decreased.[20]

Anatomic shunts that can impair oxygenation include right-to-left ventricular septal defects and right-to-left patent ductus arteriosus; these types of shunts are usually detected prior to anesthesia. Affected patients may be initially examined for variable degrees of cyanosis and may be polycythemic. Generally, repair of the defect is the only permanent solution to address the hypoxemia; however, this should not preclude oxygen supplementation in these patients.

Diffusion impairment is relatively rare in veterinary patients. Diffusion impairment may occur in patients with disease processes that cause thickening of the alveoli-blood barrier (eg, interstitial fibrosis or idiopathic pulmonary fibrosis). In a clinically normal animal, the alveoli-blood barrier is extremely thin, allowing for rapid diffusion of gas. Because the barrier is so thin, the amount of time an RBC is in the pulmonary capillary far exceeds the time required for the hemoglobin to become saturated. With diffusion impairment, this barrier is thickened, and diffusion of gas is slowed. Typically, hypoxemia is not evident until a patient is challenged with exercise or decreased inspired oxygen concentration. With severe diffusion impairment, the normal redundant commute time of RBCs in the pulmonary capillary is not sufficient for hemoglobin saturation, and exercise further decreases this transit time.[3] In veterinary patients, diffusion impairment may occur secondary to pulmonary edema or in dogs with idiopathic pulmonary fibrosis.[21] These patients should be provided with supplemental oxygen as well as with targeted treatments (eg, furosemide).

The patient of the present report was discharged with amoxicillin-clavulate (21.5 mg/kg [9.8 mg/lb], PO, q 12 h), and the owner was instructed to continue the current treatment for renal disease. Unfortunately, the patient decompensated 2 days after discharge and was examined on an emergency basis because of inappetence and vomiting. At that time, the dog had signs of abdominal pain and mild clinical dehydration. The patient was discharged with suspected gastrointestinal adverse effects related to the antimicrobial treatment and was prescribed an antiemetic. The dog again returned to the hospital 3 days later for worsening clinical signs. At that time, a serum biochemical analysis and urinalysis revealed marked renal azotemia (BUN concentration, 179 mg/dL; creatinine concentration, 12.7 mg/dL; urine specific gravity, 1.012), and the patient was hospitalized for supportive care. Leptospirosis titers were not indicative of infection, and results of bacteriologic culture of urine were negative. The presumptive diagnosis was chronic renal failure secondary to anesthesia-related hypotension, although the possibility of a renal thromboembolism was considered. The patient was subsequently euthanized because of worsening clinical signs.

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