Management of hematometra in a Boer doe

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Abstract

A 3 year old, Boer doe in late gestation was presented for an elective Cesarean section due to a previously diagnosed abdominal wall hernia. She was estimated to be 147 days pregnant, based on date of artificial insemination. Physical examination, abdominal ultrasonography, blood chemistry analyses and complete blood count were done; there was a mild anemia, but no other significant findings. Twelve hours after Cesarean section, the patient was dull and on further examination was tachycardic, tachypneic and anemic with a packed cell volume of 10%. Two liters of whole blood were transfused. Differential diagnoses included hemoabdomen or hematometra. Next day an exploratory laparotomy was performed and revealed a distended, blood-filled uterus, confirmed to be a hematometra. Medical therapy included intravenous fluids, aminocaproic acid, pantoprazole, antibiotics, and antiinflammatories. Subsequent follow up revealed that the patient had resumed normal behavior.

Keywords: Cesarean section, transfusion, alfaxalone, aminocaproic acid, hematometra

Background

Spontaneous intrauterine hemorrhage (hematometra) after Caesarean section has not been reported in goats.

Case presentation

A 77.0 kg, 3 year old Boer doe in late gestation was presented to the Iowa State University Food Animal and Camelid Hospital in early winter for an elective Cesarean section, due to a previously diagnosed abdominal body wall hernia, identified in the previous autumn after embryo recovery procedure. Doe reported to be systemically healthy with normal appetite for a diet consisting of a quart of grain twice daily and free choice hay. There was no other prior medical history.

On presentation (day 0), the doe appeared bright, alert and responsive, and had a pendulous abdomen (Figure 1). Rectal temperature (100.2ºF, normal: 100 - 103.5ºF), pulse rate (80 beats per minute, normal 70 - 90), and respiratory rate (40 breaths per minute, normal 15 - 40) were within limits. Her mucous membranes were pale pink, with a normal capillary refill time (< 2 seconds). Cardiopulmonary auscultation (normal sinus rhythm), ruminal contractions (2 per minute) and fecal production were within normal limits. Abdominal ultrasonography revealed a severe thinning of abdominal wall, ~ 24 x 13 cm, that extended from xiphoid process to inguinal region. Uterus contained 2 viable fetuses, of which 1 was positioned within hernia sac. Fetal heart rates were approximately 150 and 140 beats per minute (consistent with a reported value of multiple fetuses at 145 days gestation, 140 ± 6.4 beats per minute).[1] An abdominal dressing was placed to support hernia. Preoperative complete blood count and chemistry panel revealed mild anemia [22% packed cell volume (PCV)]. Dexamethasone (10 mg, 2 mg/ml, AgriLabs, Peachtree City, GA) was administered intramuscularly (IM) for fetal maturation and an elective Cesarean section was scheduled for the next morning.

Next day (day 1), a jugular catheter was placed. Flunixin meglumine (1.1 mg/kg, Prevail®, Vetone, Meridian, ID) was given intravenously (IV) and ceftiofur sodium (2.2 mg/kg, Naxcel®, Zoetis, Parsippany, NJ) was given IM. Moderate ketonemia (1.5 mmol/l), stable mild anemia (PCV 22%) and normal total protein (6.3 g/dl) were noted.

General anesthesia was induced with alfaxalone (2.5 mg/kg IV; Alfaxan Multidose, Jurox Inc., Kansas City, MO). General anesthesia was maintained with sevoflurane (ET_{sevo} 1.5 - 2.3%; Sandoz Inc., Princeton, NJ) in 100% oxygen. A lumbosacral epidural was performed with preservative-free bupivacaine (0.06%; AuroMedics Pharma LLC., E. Winsor, NJ) and buprenorphine (0.01 mg/kg; Buprenex®, Reckitt Benckiser Healthcare (UK) Ltd., Hull, England) for reduction of anesthetic requirement and analgesia. Lactated Ringer's solution was administered throughout the procedure. Routine monitoring equipment included electrocardiography, invasive blood pressure monitor, pulse oximetry, capnography, and temperature, and expired inhalant concentration were recorded. Spontaneous ventilation was maintained during anesthesia. Phenylephrine (0.1 - 0.3 µg/kg/min, IV; Hikma Pharmaceuticals, Columbus, OH) was titrated to maintain mean arterial pressure above 70 mm Hg. Arterial blood gas was performed and revealed a mild hypoglycemia and mild hypocalcemia, which were corrected with 2.5% dextrose supplementation in fluids and 23% calcium borogluconate (38 mg/kg, IV, Agrilabs) respectively.

Cesarean section was performed via a left-flank approach in right lateral recumbency following standard aseptic and surgical techniques. An approximately 15.0 cm dorsal-to-ventral incision was created in left flank region utilizing a #10 scalpel blade through skin, subcutaneous tissue, external abdominal oblique, internal abdominal oblique, and transversus abdominis muscle layers, and into peritoneal cavity. Uterus was exteriorized and packed off with 2 lap sponges and ~ a 12 cm incision was created in the lateral wall of left uterine horn. Two viable kids were extracted from the uterus, without complications. Immediately after delivery, kids were scored 9/10 and 10/10, respectively, utilizing a modified APGAR scoring system (Table). Uterine incision was closed utilizing 0 polydioxanone suture (PDS II®, Ethicon, Basking Ridge, NJ) in Utrecht pattern. A second layer was inverted with the same 0 PDS in Utrecht pattern over initial uterine closure. Peritoneum and transversus abdominis were closed in a simple continuous pattern using 0 PDS. Internal abdominal oblique and external abdominal oblique were then closed in a simple continuous pattern using 0 PDS. Subcutaneous layer was closed using 0 PDS in a simple continuous pattern and skin was closed using 0 Braunamid (Tuttlingen, Germany) in a ford-interlocking pattern. A liquid aluminum bandage was applied to the incision.

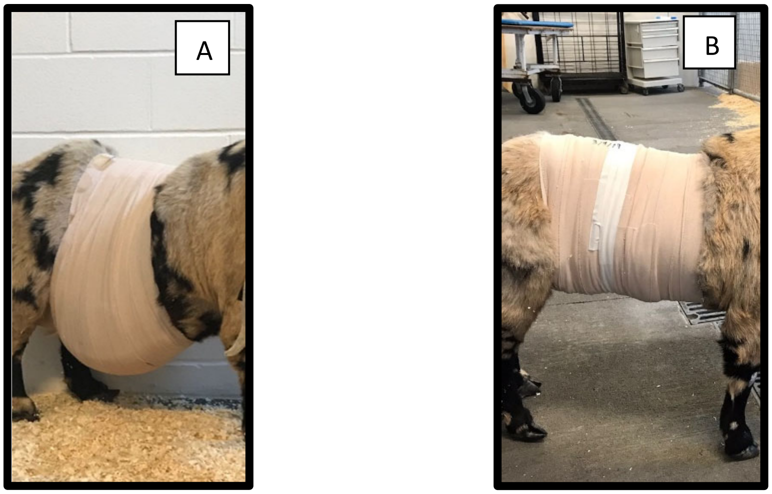

Figure 1. At presentation, doe had an extensive ventral abdominal wall hernia and was in late term gestation. Ventral body wall was supported with bandaging material (A). After Cesarean section, bandaging material was reapplied for continued support and to facilitate tissue contraction and development of a fibrous ring for future hernia repair (B).

Parameter	Score 0	Score 1	Score 2
Heart Rate	<100 beats/minute	100-120 beats/minute	> 120 beats/minute
Respiratory Effort	< 30 breaths/minute, no vocalization,	30-40 breaths/minute, mild vocalization	>40 breaths/minute, vocalization
Reflex Irritability	Absent	Mildly present	Vigorously present
Motility	Flaccid	Some flexion	Active motion
Mucous Membrane Color	Cyanotic	Pale	Pink

Table. Modified APGAR scoring system (based on Veronesi et al: [2]) used for evaluation of kids after alfaxalone administration. Scores of 7 - 10 indicate no distress; 4 - 6 moderate distress and 0 - 3 severe distress.

Patient recovered uneventfully from general anesthesia. Due to inadequate colostrum supply and severity of the hernia, it was elected to maintain her 2 kids on bottle feedings. Patient received flunixin meglumine (1.1 mg/kg, IV; Vetone) and ceftiofur sodium (2.2 mg/kg, IM; Zoetis) every 12 hours after surgery. Kids remained bright and alert and consumed colostrum replacer readily.

Approximately 12 hours after Cesarean section, patient exhibited frequent vocalization, rapid decline in mentation, tachypnea and pale mucous membranes. Severe anemia was documented (PCV 10%) and she continued to decompensate over the next several hours, becoming anorexic, hypothermic, tachycardic, tachypneic, hyperglycemic, hypoproteinemic and hyperlactatemic. Mild abdominal effusion was noted on transabdominal ultrasound. Patient received supplemental oxygen via face mask (5 liters/minute), resuscitative fluid boluses, and ε-aminocaproic acid (40 mg/kg, IV, American Regent, Shirley, NY). Additionally, 2 liters of whole blood was transfused following standard transfusion protocol, with no adverse reactions, as described below.

A pretransfusion dose of flunixin meglumine (1.1 mg/kg, IV) was given. During transfusion, patient's temperature, heart rate, and respiratory rate were monitored initially every 5 minutes, with a rate of 385 ml/hour (5 ml/kg/hour). After no initial signs of reaction, the rate was increased to 770 ml/hour (10 ml/kg/hour) and vitals were recorded every 10 minutes. To finish the transfusion, the patients' rate was increased to 1540 ml/hour (20 ml/kg/hour), with vital parameters recorded every 15 minutes. Patient was closely monitored for transfusion reactions including facial swelling, urticaria, fever, respiratory distress, anaphylactic reactions, and piloerection. Although no adverse reactions were recorded, respiratory rate remained elevated throughout transfusion and the patient began to cough 20 minutes into transfusion, which ceased 10 minutes later. Following first liter of transfusion, her PCV increased to 13%. Abdominal ultrasonography at this point revealed significant effusion (suspected to be hemorrhage) within the abdominal cavity in the vicinity of uterus. There was clinical uncertainty whether abdominal ultrasonography reflected a hemoabdomen due to uterine rupture, or a hematometra. An abdominocentesis was inconclusive.

Exploratory laparotomy was elected to determine cause of anemia and a second liter of whole blood transfusion was initiated. General anesthesia was induced with ketamine (2 mg/kg, IV; Zetamine™, VetOne, Boise, ID) and propofol (2 mg/kg IV; PropoFlo™, Zoetis) and maintained on sevoflurane (ET_{sevo} 0.9 -1.3%) in 100% oxygen. A ketamine (20 µg/kg/min) and fentanyl (0.05 µg/kg/min; Hospira Inc., Lake Forest, IL) were given for intraoperative analgesia at constant rate infusion. Routine monitoring equipment was used as previously described. To maintain normotension, a dopamine (2 µg/kg/min; Hospira Inc., Lake Forest, IL) was given during the procedure at constant rate infusion. Arterial blood gas revealed mild hypocalcemia post-blood transfusion; therefore, 23% calcium borogluconate (56 mg/kg, IV) was given.

Patient was placed in lateral recumbency and the previous surgical incision was reopened to expose abdominal contents. There was no evidence of excessive free fluid or blood in the abdominal cavity. Hematometra was confirmed via fine needle aspiration. Remainder of the abdominal exploration was unrewarding. Abdominal incision was closed in a routine fashion.

Patient recovered well from general anesthesia with normalization of her vital parameters, mentation, and activity. A balanced polyionic fluid with 20 mg/kg of aminocaproic acid was continued. Pain was managed with morphine (0.1 mg/kg, IV) and flunixin meglumine (1.1 mg/kg, IV). Nasal oxygen supplementation was discontinued. On day 3, doe was quiet but alert and resting comfortably. Her appetite, mentation, and vital physical parameters remained normal. Her last dose of aminocaproic acid was given (4 doses total) and intravenous fluids discontinued. Tarry fecal matter was noted and a strong positive fecal occult blood test confirmed gastrointestinal bleeding. Doe was started on pantoprazole (1 mg/kg IV, Protonix®, Pfizer, New York, NY). At this time the patient had normal lactate, glucose, and ketones. Her PCV was 22% with a total protein of 6.2 g/dl; however, a newly developed hyperfibrinogenemia was noted (600 mg/dl). This elevation was attributed to surgical inflammatory process occurring within the uterus after Cesarean section.

On the third day after initial surgery, a small amount of blood-tinged vaginal discharge was observed. Her PCV remained stable at 25% with a total protein of 6.8 g/dl. Her abdominal hernia support bandage was changed and her incision was evaluated to be healing appropriately. On day 6, flunixin meglumine was discontinued and pantoprazole was discontinued after multiple negative fecal occult blood tests. Patient continued to have bloody vaginal discharge that waxed and waned from mild to prominent over next several days. Patient's intravenous catheter was removed on day 8 of hospitalization. At this time, PCV remained stable at 26%. Patient continued to have normal vital parameters and her appetite and energy were appropriate. On the evening of day 9, patient became febrile and tachycardic. Flunixin meglumine (1.1 mg/kg, IV) and procaine penicillin G (22,000 IU/kg, IM, AgriLabs) were administered every 12 hours. Patient did not have any other abnormal signs at this time. Her udder was not swollen, painful, or hot on palpation. Patient continued to have mild bloody vaginal discharge but her appetite and attitude remained adequate. Despite continued mild bloody vaginal discharge, patient showed marked clinical improvement. Normal uterine involution was observed on transabdominal ultrasonography at this stage with small amount of fluid. No free abdominal fluid was observed and surgical site was healing appropriately.

On day 9, a complete blood count revealed persistent hyperfibrinogenemia, mild mature neutrophilia with toxic changes, and anemia. On day 10, transabdominal ultrasonography findings of uterus remained unchanged and her PCV improved to 22%. Uterine lavage was performed and a minimal amount of brown/red tinged mucus-like fluid was recovered. It was suspected that fetal membranes were autolyzed and passing appropriately within the vaginal discharge observed.

On day 12, ceftiofur sodium was discontinued. Patient continued to have stringy, bloody vaginal discharge but her clinical condition remained stable in the subsequent days. There appeared to be no further development of metritis, mastitis or concurrent infection.

Treatment

Treatment included Cesarean section, hypovolemic shock management, blood transfusion, pain management, antibiotics, and aminocaproic acid therapy. Twelve hours after Cesarean section, patient received supplemental oxygen via mask (5 liters/minute), intravenous fluids, and aminocaproic acid. Two liters of whole blood was transfused; her PCV prior to first transfusion was 10% and then increased to 13%. After second transfusion, PCV increased to 19%.

Outcome

Patient experienced intra-uterine hemorrhaging following Cesarean section and a transfusion of 2 liters of whole blood was necessary for stabilization. An exploratory laparotomy was performed revealing a hematometra. Patient was maintained on systemic broad-spectrum antibiotics, a nonsteroidal antiinflammatory and a proton pump inhibitor throughout the course of hospitalization. Uterine involution was monitored periodically using transabdominal ultrasound. Patient was noted to resume normal behavior and was later determined to be a good surgical candidate for an abdominal hernia repair.

Discussion

Hematometra following Cesarean sections has apparently not been reported in goats. There are reports of spontaneous uterine hemorrhage in other veterinary species, often related to the presence of cystic endometrial hyperplasia. Severe hematometra was reported in a German Shepherd dog with cystic endometrial hyperplasia. An abdominal ultrasonography demonstrated that uterine body and cranial vaginal lumen were fluid-filled and containing hyperechoic, polyploid masses suspected to be blood clots.[3] In the current case, abdominal ultrasonography led to suspicion of an acute hemorrhage due to visualization of fluid within abdomen in the location of uterus. Diagnostic tests supported an acute hemorrhage, but the source was unknown. With evidence of acute hemorrhage, an exploratory laparotomy was necessary to confirm the source of bleeding. In this case, the procedure revealed a distended, fluid-filled uterus. This same presentation was observed in the case of a German Shepherd dog where the procedure revealed a mildly enlarged uterus. However, an ovariohysterectomy was performed on the dog and histopathology confirmed a severe, cystic, endometrial hyperplasia and pyometra complex.[3] Cases of canine hematometra have also been associated with uterine torsion or other uterine disease such as a pyometra, in addition to toxicities such as rodenticide exposure.[4] Perhaps many cases of canine hematometra are asymptomatic and uncomplicated until they lead to uterine torsion or other uterine pathology.[5] Spontaneous hemorrhage after Cesarean section in goats has not been reported. It is not known at this time what was the exact mechanism for development of hematometra in this doe. Fetal membranes were not forcibly removed during surgery, and uterus was closed in routine fashion. No significant hemorrhage was noted during surgery. Perhaps the nature of induction contributed to this finding.

This case involved hematometra in a goat with a concurrent severe abdominal wall hernia. Goats often have forms of hernias, both acquired and congenital. Abdominal, inguinal and scrotal hernias are usually acquired whereas umbilical hernias are congenital in this species.[6] Patient in this case had an acquired, severe abdominal hernia. Although a very rare complication, a hernia may interfere with normal parturition. Due to the extent of the hernia in this doe, an elective Cesarean section was recommended, due to the risk of complications with vaginal delivery as a gravid uterus can become entrapped in an abdominal hernia, making vaginal delivery difficult.[6] Presence of an abdominal hernia can pose the risk of uterine incarceration or strangulation.[7] Other risks that have been reported in humans with a gravid uterus and abdominal hernia include abortion, preterm or dysfunctional labor, and intrauterine growth retardation leading to fetal death.[7] Risk of uterine strangulation is an indication for early hospitalization and elective Cesarean section, with subsequent hernia repair.[8] By performing an elective Cesarean section, these complications may be avoided.

Selection of an appropriate anesthesia protocol for Cesarean sections is important to minimize risks to doe and kid(s). Alfaxalone is a neurosteroidal anesthetic agent characterized by a smooth and rapid induction, short duration of action, and quiet recovery.[9] Alfaxalone does not accumulate in tissues at clinical doses, making this useful in food animal species.[9] Alfaxalone's mechanism is a synthetic neuroactive steroid that acts on $GABA_A$ receptors in the central nervous system producing general anesthesia.[9] It is a reliable and smooth induction agent in sheep, goats, and calves.[10] In the present case, use of alfaxalone was demonstrated to be clinically useful in inducing anesthesia. Alfaxalone has not caused major adverse effects in previous studies, and this agent can provide excellent induction or short-term anesthesia as a single bolus.[10] Alfaxalone is associated with dose-dependent and administration rate-dependent respiratory depression and arterial vasodilaton, although these effects are transient and mild at clinically useful doses. However, these cardiovascular and respiratory depressant effects can become significant in critically ill patients. In goat kids, alfaxalone appeared to be a suitable induction agent.[11] Alfaxalone does not appear to have detrimental effects in neonates when used as an induction agent prior to Caesarean section. Alfaxalone was associated with higher APGAR scores and overall neonatal vitality in puppies during the first 60 minutes after delivery compared to propofol; however, 3 month survival rate did not differ between groups.[12] Two kids in this case had APGAR scores of 9 and 10 respectively, indicating that alfaxalone may be safe for kids during a caprine Cesarean section. Drugs that should be avoided include xylazine, ketamine, and methoxyflurane due to the association of increased risk for neonatal and maternal mortality.[13]

Aminocaproic acid is an antifibrinolytic agent that has been used in veterinary medicine in cases of acute hemorrhage.[14] Hyperfibrinolysis has been shown to occur in dogs with severe, acute blood loss and antifibrinolytic agent therapy may be indicated in these cases.[14] Greyhounds in particular are predisposed to excessive fibrinolysis after surgery. Aminocaproic acid has been beneficial as a perioperative measure in this patient population.[14] Generally, any animal at risk for hemorrhage after surgery may benefit from antifibrinolytic agents as treatment with aminocaproic acid has been shown to enhance clot strength in patients with hyperfibrinolysis.[14] Our patient was given injectable aminocaproic acid after a 50% decrease in her PCV 12 hours after surgery. A loading dose of 40 mg/kg was administered IV, followed by 3 additional doses of 20 mg/kg. Each dose was diluted in 1 liter of balanced polyionic solution and given as a constant rate infusion. Aminocaproic acid has been well tolerated by dogs, but its use has not been reported in goats. No adverse effects were observed in dogs for any dose of aminocaproic acid.[14] Aminocaproic acid as a procoagulant therapy, as described for other species, appears to be a potentially useful adjunct therapy for anemic goats due to acute hemorrhage.

Currently no prospective studies regarding the use of pantoprazole in goats exist. Efficacy of pantoprazole in alpacas[15] has been reported and has been shown to increase pH of third compartment. Case reports involving other ruminant species demonstrate the use of pantoprazole in a goat,[16] a sheep[17] and yak bulls[18] with no perceived complications. In humans, long-term use of pantoprazole has been associated with neutropenia and thrombocytopenia,[19] which were not observed in our doe, although the history of transfusion could complicate these observations. Based on this case and other ruminant cases, pantoprazole may be a safe short-term therapy for suspected abomasal ulcers.

In this case, patient received 2 liters of whole blood, with a resulting increase in PCV from 10 to 19%. No transfusion reactions were noted (reported transfusion reaction rate was 16% in small ruminants in 1 study).[20] This case highlights other issues of management of the doe with respect to Cesarean sections. While not common, the need for a transfusion may require access to donors or blood products.

While not commonly used, multiple drugs utilized for the management of this case were not labelled for goats and were thus used in an extra-label fashion. Withdrawal times for alfaxalone and aminocaproic acid for goats are required by the Food Animal Residue Avoidance Databank. No tissue residue data has been recorded to base a withdrawal time for alfaxalone in goats. However, the drug is rapidly cleared from plasma and plasma half-lives in cats, dogs, and horses range from 30 minutes to 1.5 hours for alfaxalone. Furthermore, no tissue or residue data has been recorded for aminocaproic acid in any food producing species. In general, there is limited literature on aminocaproic acid. There has been only one pharmacokinetic study in horses demonstrating plasma half-life of 2.3 hours following a 20 minute CRI at 3.5 mg/kg/minute. Aminocaproic acid is mainly used in humans and the drug concentrations were equal or higher in milk than plasma. A minimum of a 6 week withdrawal interval has been recommended for this drug in the past, but further research is required regarding testing for aminocaproic acid.

Learning points

- While not common, spontaneous hemorrhage following Caesarean section should be considered as a differential in weak or anemic goats after uterine surgery.
- Alfaxalone did not appear to have detrimental effects to neonatal kids when used as an induction agent prior to Caesarean section.
- Aminocaproic acid procoagulant therapy, as described for other species, appeared to be a potential useful therapy for goats with acute and ongoing blood loss from hematometra.

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(Editor's note: Online edition of the manuscript has color photographs)