Theriogenology Question of the Month

The American College of Theriogenologists sponsors this feature. Readers of the JAVMA are invited to submit contributions. Contributions should provide a learning exercise about theriogenology. A specific question should be posed for the readers. The author's answer to the question and a brief discussion should be presented. Possible topics include commonly seen problems in domestic or exotic animals. Herd problems in dairy and beef cattle, sheep, goats, horses, and exotic hoofstock, problems in kennels or catteries, or flock problems in domestic and exotic fowl also are appropriate. Please contact Dr. Craig A. Smith, Associate Editor (800/248-2862, ext 6764, or FAX 847/825-9329), for further details.

History

A 48-month-old female Labrador Retriever was examined 2 days after parturition. The bitch had a malodorous serosanguineous vaginal discharge and was lethargic. The dog vomited on the morning of our initial examination.

Reproductive history of the bitch included 2 pregnancies at 24 and 36 months of age. For the first pregnancy, the bitch whelped prematurely at 60 days of gestation (as determined on the basis of estimation of the luteinizing hormone [LH] surge by evaluation of serial serum progesterone concentrations to detect the initial increase to >2 ng of progesterone/mL). At 59 days of gestation, a green vaginal discharge (ie, uteroverdin) was detected. The bitch gave birth to 11 puppies, 8 of which were stillborn. Bacterial culture of a fetal membrane (ie, placenta) yielded pure growth of a colony of nonenteric gram-negative rods. Premature labor was attributed to bacterial placentalitis and subsequent metritis.

For the second pregnancy, the dog whelped at 65 days of gestation (as determined on the basis of estimation of the LH surge by evaluation of serial serum progesterone concentrations). During a 5-hour period, the bitch gave birth to 8 puppies, the last of which was stillborn. Repeated uterine monitoring and detection of fetal heart rate were used to document the progression of labor, evaluate fetal distress, and determine dystocia. Parturition was medically assisted via SC administration of 2 units of oxytocin. A 1-hour period, the bitch gave birth to 8 puppies. Secondary uterine inertia was diagnosed by use of uterine monitoring 10 hours after onset of stage-1 labor. Uterine inertia was medically treated by SC administration of calcium gluconate (total dose, 13.95 mEq) and oxytocin (total dose, 6.5 units). Manual assistance (per vagina) was required for delivery of all puppies. The bitch was constantly monitored during whelping. Observers detected passage of only 2 fetal membranes; the remaining 6 fetal membranes were presumably retained.

The bitch was current on all vaccinations (distemper, canine adenovirus type-2, parvovirus, parainfluenza, rabies, and Bordetella bronchiseptica) and was receiving regular heartworm prophylaxis. Serologic testing for brucellosis had been completed every 6 months; all test results were negative. The bitch had a medical history of chronic otitis externa associated with Malassezia spp, but no aural treatments or other medications had been administered during pregnancy. Prior to our initial examination, the bitch had received each of several medications 1 time on the advice of a staff veterinarian because of the dystocia and presumed retained fetal membranes, including carprofen (2 mg/kg [0.9 mg/lb], PO), enrofloxacine (4.3 mg/kg [2 mg/lb], SC), cefazolin (27 mg/kg [12.3 mg/lb], SC), prostaglandin F2alpha (0.1 mg/kg [0.045 mg/lb], SC), and lactated Ringer’s solution (400 mL, SC).

Abnormal findings on physical examination were limited to a rectal temperature of 41.0°C (105.8°F), malaise, and a moderate amount of malodorous serosanguineous vaginal discharge. The mammary glands and milk were judged to be normal.

All puppies appeared to be clinically normal. Weight gain of the puppies during the first 48 hours after birth was adequate.

Differential diagnoses for the febrile condition included infection (bacterial, fungal, viral, protozoal, or rickettsial), inflammation (peritonitis) or immune-mediated disease, hypocalcemia, neoplasia, and an excessively hot ambient temperature. Differential diagnoses for the malodorous serosanguineous vaginal discharge after whelping included retained fetal membranes, metritis, and a retained uterus. Malaise was considered to be a nonspecific clinical sign attributed to systemic illness.

Analysis of results of a CBC revealed anemia (Hct, 35.1%; reference range, 37% to 55%) and leukopenia (total WBC count, 2,200 cells/mm3; reference range,
6,000 to 17,000 cells/mm³) with granulocytopenia (1,900 cells/mm³; reference range, 3,500 to 12,000 cells/mm³). Serum biochemical analysis revealed hypoalbuminemia (2.3 g/dL; reference range, 2.7 to 3.8 g/dL), hypoproteinemina (5.16 g/dL; reference range, 5.2 to 8.2 g/dL) with a serum globulin concentration within the reference range, and a decrease in BUN concentration (5.9 mg/dL; reference range, 7.0 to 27.0 mg/dL). Additional indicators of hepatic function (ie, glucose, cholesterol, and bilirubin concentrations) were within the reported reference ranges. Urine specific gravity was 1.010; results of examination of sediment were unremarkable. Abdominal ultrasonography was performed (Fig 1 and 2).

**Question**

What is the cause of this bitch’s illness? *Please turn the page.*
Answer

Results of abdominal ultrasonography were consistent with acute metritis secondary to retained fetal membranes and a retained nonviable fetus.

Discussion

It is important to monitor vital functions, appetite, and demeanor of postpartum bitches on a daily basis to enable early detection of illness. Any postpartum bitch that has clinical signs of lethargy, anorexia, or vomiting or has a fever (≥39.7°C [≥103.5°F]) should be evaluated by a veterinarian. Initial differential diagnoses for sick postpartum bitches include mastitis, hypocalcemia, and acute metritis, which can be associated with a retained fetus or retained fetal membranes. Ultrasonographic evaluation of the reproductive tract is helpful to distinguish these conditions. The normal involuting postpartum uterus of a medium-size dog has a luminal diameter of approximately 4 cm and hypoechoic contents. Retained fetal membranes can appear as an organized area of hyperechogenicity within the lumen of the uterine horns. Metritis should be suspected when the uterine wall is thickened or unusually irregular. A hyperechoic appearance of the mesentery is of concern because it may indicate focal peritonitis and loss of uterine integrity (ie, rupture of the uterine wall).

A bitch with a retained fetus will typically develop signs of systemic illness, such as anorexia, vomiting, and lethargy, 2 to 4 days after whelping. Poor maternal behavior can also be evident. Clinical manifestations associated with sepsis can result from ascending bacterial contamination of the uterus while the cervix is open during the periparturient period, resulting in endotoxemia or septicemia.

Commonly, owners report that a fetal skeleton count was completed during late gestation by use of abdominal radiographs and that the bitch whelped the designated number of puppies. As illustrated here, a retained fetus should be considered as a differential diagnosis in any sick postpartum bitch until abdominal imaging can be completed. Litter size determined by examination of abdominal radiographs taken during late gestation may not be a reliable indicator that a bitch has subsequently completed whelping and expelled all fetuses.

Serosanguineous postpartum vaginal discharge (lochia) is a normal finding and may continue for up to 16 weeks after parturition in clinically normal bitches. Some individuals may consider normal lochia to have an unpleasant odor; however, vaginal discharge associated with retained fetal membranes or a retained fetus typically has a putrid odor.

It is generally accepted that ovarian hormones, specifically estrogen, have a substantial impact on uterine motility in bitches. In 1 study, exogenous administration of oxytocin and prostaglandins induced similar effects on uterine motility of dogs within each phase of the estrous cycle, with the strongest response during estrus. In most species, parturition is associated with a decrease in serum progesterone concentrations and an increase in serum estrogen concentrations, resulting in upregulation of expression by oxytocin receptors and an increase in binding affinity for oxytocin to its receptors. Contrary to parturition in other female animals, parturition in bitches is not associated with an increase in serum estrogen concentrations; thus, the exact relationship between ovarian hormones and periparturient uterine physiologic characteristics is not clear.

Although prostaglandins and oxytocin have similar effects on uterine motility during diestrus, prostaglandins are preferred for use in evacuating uterine contents because they also have luteolytic activity and may promote cervical relaxation. In postpartum animals, prostaglandin use is preferred for inducing uterine evacuation because of the variation in expression of oxytocin receptors during that period.

Bitches with a retained fetus typically are treated surgically. Medical treatment (administration of prostaglandins) of bitches to cause expulsion of a retained fetus has not been clearly described. Prostaglandins have been used for uterine evacuation in bitches with pyometra or as an abortifacient in pregnant bitches. Bitches are more resistant to the luteolytic effects of prostaglandins, compared to other species. It is important to mention that the therapeutic index for prostaglandin $F_2\alpha$ in dogs is narrow, with a lethal dose for natural prostaglandins of 5.13 mg/kg (2.33 mg/lb). Information regarding the minimum effective dose to induce uterine contractions and uterine evacuation is unknown.

In contrast to pyometra in bitches, acute metritis secondary to a retained fetus has not been associated with cystic endometrial hyperplasia and develops when the serum progesterone concentration is low. In bitches with reproductive importance, prostaglandin administration may be used to medically evacuate a retained fetus and maintain reproductive viability while minimizing morbidity. Risks of prostaglandin administration that must be considered and thus monitored for include uterine rupture, peritonitis, coagulopathies, and sepsis and its consequences (eg, acute renal failure and organ dysfunction). The minimal degree of monitoring should include serial physical examinations, abdominal ultrasonography, CBC and serum biochemical analyses, and evaluation of urine production. At a minimum, adjunctive medical treatments should include IV administration of fluids and antimicrobials. Consideration should also be given to monitoring the health and weight gain of neonatal puppies.

Outcome

In the bitch described here, abdominal ultrasonography revealed that both uterine horns were involving but had hyperechoic contents (Fig 3). The lumen of the uterine horns was 4 cm in diameter at the widest point. A single fetus was located in the body of the uterus cranial to the pelvic brim; we did not detect a fetal heartbeat (Fig 4). Furthermore, there was no evidence of peritonitis (no signs of abdominal pain, no evidence of free fluid in the abdominal cavity, and the mesentery was not hyperechoic).

Intravenous administration of fluid (consisting of lactated Ringer’s solution supplemented with 14 mEq of potassium chloride/L) was administered at the rate of 6 mL/kg/h (2.7 mL/lb/h) for 24 hours. The hypoalbuminemia and mild decrease in total protein concentration were attributed to a negative acute-phase protein response. The low BUN concentration detected on serum
biochemical analysis was suggestive of secondary nephrogenic diabetes insipidus attributable to bacterial endotoxins. The mild anemia was considered to be a normal physiologic condition for a postparturient bitch, and treatment for that condition was not needed. Ampicillin (22 mg/kg [10 mg/lb], IV, q 8 h) and enrofloxacin (10 mg/kg [4.5 mg/lb], PO, q 12 h) were administered because of the leukopenia and granulocytopenia, which were attributed to infection and uterine sequestration of WBCs. Enrofloxacin and ampicillin were used because of their efficacy against Escherichia coli, streptococci, and staphylococci. Prostaglandin F2α was administered (0.1 mg/kg, SC) 3 times during the hours of 8 AM to 5 PM for several days in an attempt to induce fetal expulsion. Metoclopramide (0.1 mg/kg) and famotidine (0.5 mg/kg [0.23 mg/lb]) were administered twice each day in anticipation of nausea and secondary esophagitis associated with prostaglandin F2α administration. The dose of prostaglandin F2α used in the bitch described here was not associated with any appreciable adverse effects.

A physical examination and abdominal ultrasound were conducted prior to each prostaglandin F2α injection to evaluate for evidence of peritonitis. Additional monitoring included measurement of rectal temperature every 4 hours; CBC and biochemical analyses every 24 hours; and evaluation of appetite, vomiting, maternal behavior, and demeanor.

Rectal temperature was 37.9°C (100.3°F) 12 hours after initiating treatment. Analysis of results of a CBC and biochemical analyses after administration of 2 doses of prostaglandin F2α revealed anemia (Hct, 33.7%) and leukopenia (total WBC count, 5,300 cells/mm³) attributable to lymphopenia (200 cells/mm³; reference range, 1,200 to 4,500 cells/mm³) and monocytopenia (200 cells/mm³; reference range, 300 to 1,000 cells/mm³). Analysis of results of serum biochemical analyses revealed continued hypoalbuminemia (2.08 g/dL), hypoproteinemia (4.8 g/dL), and a low BUN concentration (3.5 mg/dL). The retained fetus was expelled after the fifth injection of prostaglandin F2α (30 hours after initiation of treatment). Results of a CBC performed 12 hours after fetal expulsion revealed that the Hct and WBC counts were within the reference ranges (Hct, 48.8%; total WBC count, 11,900 cells/mm³) with lymphopenia (800 cells/mm³) and monocytopenia (100 cells/mm³). Analysis of results of serum biochemical analysis at that time revealed mild hypoalbuminemia (2.2 g/dL) with total protein (5.2 g/dL) and BUN concentrations (9.0 mg/dL) within the reference range.

All puppies remained healthy during treatment of the dam. Puppies were weaned 5 weeks later.

References