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 847/925-9329), for further details.

History

A 6-year-old 682-kg (1,500-lb) Angus cow was admitted to our veterinary teaching hospital with a history of being anorectic and seeking isolation from the remainder of the herd during the preceding 3 days. The cow had been artificially inseminated 6 months prior to admission. Vaccination history for the cow was unknown.

Physical examination revealed that the cow was afebrile and tachypneic. The cow also had black tarry diarrhea and strained to urinate. Rectal palpation revealed that the cow was pregnant; gestational age (6 months) was consistent with the date of artificial insemination. Vaginoscopic examination revealed 3 polyp-like masses on the left lateral vaginal wall in the region of the external cervical os. The masses were 2 to 4 cm in size; their color was similar to that of the vaginal mucosa. Manual examination of the vagina revealed that the masses had normal texture for a soft tissue structure. Transabdominal ultrasonography performed with a 5.0-MHz linear-array transducer revealed a fetus, fetal fluids, and placentomes, but a fetal heartbeat was not detected. Transrectal ultrasonography revealed that the cervix and wall of the uterine body were thickened and hyperechoic.

Analysis of results of a CBC revealed that the cow had a low RBC count (4.67 $\times$ 10^6 cells/µL; reference range, 5 $\times$ 10^6 to 10 $\times$ 10^6 cells/µL), a low PCV (23%; reference range, 24% to 48%), leukocytosis (35.5 $\times$ 10^3 cells/µL; reference range, 4 $\times$ 10^3 cells/µL to 12 $\times$ 10^3 cells/µL), neutrophilia (6.9 $\times$ 10^3 cells/µL; reference range, 0.6 $\times$ 10^3 cells/µL to 4 $\times$ 10^3 cells/µL), lymphocytosis (27 $\times$ 10^3 cells/µL; reference range, 2.5 $\times$ 10^3 cells/µL to 7.5 $\times$ 10^3 cells/µL), and monocytosis (1.4 $\times$ 10^3 cells/µL; reference range, 0 to 0.8 $\times$ 10^3 cells/µL). Morphologic examination of WBCs revealed a few large lymphoblasts.

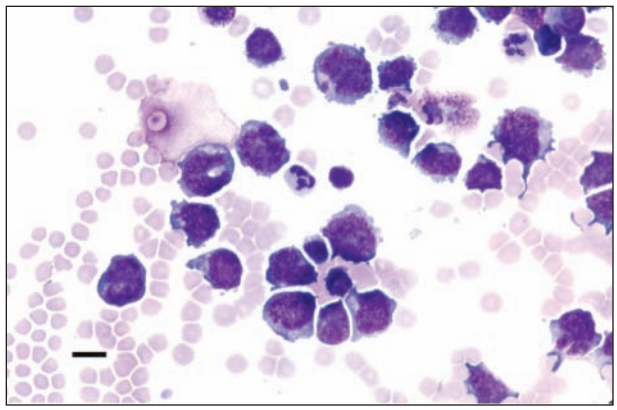

Figure 1—Photomicrograph of peritoneal fluid obtained from a 6-year-old cow that was at 6 months of gestation, was anorectic, and had stranguria and black tarry diarrhea. Wright stain; bar = 10 µm.

Serum biochemical analysis revealed hypoglycemia (54 mg/dL; reference range, 70 to 100 mg/dL), high concentrations of BUN (24 mg/dL; reference range, 9 to 21 mg/dL) and creatinine (3.1 mg/dL; reference range, 1.1 to 1.8 mg/dL), and high activity of creatine kinase (813 U/L; reference range, 0 to 350 U/L).

Urinalysis revealed a low specific gravity (1.004; reference range, 1.020 to 1.040), proteinuria (100 mg/dL; reference range, < 0.01 mg/dL), a large amount of hemoglobin, and numerous squamous epithelial cells. A biopsy specimen was obtained from 1 of the vaginal masses and submitted for histologic examination, and a sample of peritoneal fluid was obtained for cytologic analysis (**Fig 1**). Ceftiofur was administered to the cow (2.2 mg/kg [1 mg/lb], SC, q 24 h, for 3 days).

Question

What is the most likely cause for the vaginal masses and thickened, hyperechoic uterus and cervix in this pregnant cow? ***Please turn the page.***

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Answer

Lymphosarcoma infiltrating the uterus, cervix, and vagina.

Outcome

Because of the grave prognosis and inability to salvage the cow for slaughter, the owner elected to donate the cow to our facility. For instructional purposes, an exploratory laparotomy was performed via the right flank with the cow in a standing position. Abdominal exploration confirmed a thickened uterine wall and distended urinary bladder. Intra-abdominal ultrasonography of the uterus with a 5.0-MHz linear-array transducer revealed a fetal heartbeat. The cow was euthanatized and submitted for necropsy.

Results

Examination of the biopsy specimen obtained from 1 of the vaginal masses revealed a homogenous population of round, neoplastic, lymphocytic cells. The sample of peritoneal fluid contained RBCs and nucleated cells (90% large lymphocytes with mitotic figures, 10% neutrophils, and a few eosinophils; Fig 1). Serologic testing for **bovine leukemia virus (BLV)** yielded positive results. These findings were consistent with lymphosarcoma.

Necropsy revealed 3 pedunculated, firm, tan, homogeneous masses (4 to 7 cm in diameter) in the left lateral wall of the vagina in the region of the external cervical os. The cervix and wall of the uterine body were severely thickened (2 to 3 times the typical thickness) by a tan, homogeneous mass. The urinary bladder was severely distended and filled with clear urine. The ureters were dilated (2 to 3 times their typical size), and the renal pelvis of each kidney was moderately dilated. A brown friable mass (5 cm in diameter) was located on the capsular surface of the right kidney, extending approximately 1 cm into the cortex. A firm, homogenous, tan mass (20 × 15 × 7 cm) was found in the wall of the right atrium. All lymph nodes that were examined were enlarged (2 to 3 times their typical size) and firm and had a mottled tan-red appearance.

Histologic examination of uterine tissues revealed a normal mucosa and submucosa, but most of the myometrium was invaded and replaced by homogenous sheets of neoplastic masses. Neoplastic invasion was also apparent in the abomasum and epaxial and longissimus muscles.

Discussion

Masses in the uterus and cervix must be differentiated from other causes of uterine and cervical enlargements. Enlargements of the uterus and cervix can be attributable to tumors (fibromas, fibrosarcomas, leiomyomas, leiomyosarcomas, and carcinomas), fat necrosis, fetal mummification, or inflammation. In the cow reported here, enlargements of the uterus and cervix were caused by lymphosarcoma. The combination of the advanced gestation and large neoplastic masses in the pelvic canal created pressure on the urethra, which restricted urinary outflow and resulted in stranguria. On the basis of age of the cow and results of serologic testing, cytologic examination, gross necropsy, and histologic examination, the tumor was diagnosed as leukosis associated with BLV.

The cow reported here was pregnant (6 months of gestation), as determined on the basis of the history (date of insemination) and rectal examination. We were not able to verify viability of the fetus during initial examinations, and it was only during exploratory abdominal surgery that we confirmed the fetus was viable. However, pregnant cattle with lymphosarcoma infiltrating the uterus usually deliver small or nonviable calves when they are affected several weeks or months before term. Cattle that are < 6 months of gestation seldom give birth to viable calves.[1]

Lymphosarcoma in adult cattle caused by the retrovirus BLV is the most common neoplastic disease of cattle > 2 years old.[2] The virus resides within lymphocytes, which provide protection from an animal's immune defenses. Once infected, an animal is infected for life. Although all breeds of cattle are susceptible, dairy cattle are more frequently infected, presumably because of their close confinement. Surveys conducted during the past 15 years found that 2% to 10% of dairy cattle and 1% to 6% of beef cattle were infected with BLV.[2] Within herds, 0% to > 50% of cattle in specific dairy herds and 0% to 20% of cattle in specific beef herds can be infected. The proportion of herds infected with BLV varies among states but is high in the southern United States.[2] Less than 1% of BLV-infected cattle will develop lymphosarcoma. We are not aware of any effective treatments for lymphosarcoma; therefore, the prognosis is grave.[1]

Because BLV is found in lymphocytes and rarely as a free virus, transmission of infected lymphocytes to a susceptible animal is necessary for infection. Three common routes of transmission include the transfer of infected blood, consumption of contaminated colostrum or milk, and transplacental transfer of the virus. Management procedures that contribute to the transfer of infected blood include use of the same needle and syringe to perform multiple vaccinations or collection of several blood samples. Similarly, dehorning, tattooing, ear tagging, castrating, or any other means for the use of blood-contaminated surgical equipment on multiple cattle could transmit the virus.[3] Biting flies have been implicated in the spread of BLV among cattle. Cattle in the southern United States are at high risk for viral exposure because of the almost continuous exposure to biting, flying insects.[4]

Newborn calves can be infected orally but are probably resistant via the oral route of infection by 3 weeks of age. The oral route does not serve as a means for infection of adult cattle. Adult cows can be infected by the instillation of infected lymphocytes into the reproductive tract, but semen mixed with the inoculum may have an inhibitory effect on transmission; in addition, susceptibility of the genital tract of cows may decrease during estrus.[3] The virus has been experimentally transmitted by inoculation of large quantities of blood obtained from BLV-infected cattle into the rectums of susceptible cattle.[5] However, the likelihood of transfer of large volumes of blood during routine per rectal palpation is minimal and probably not sufficient to cause infection; therefore, the risk of transmission via this

route is low, and BLV is not transmitted or transmitted only rarely via per rectal palpation typically performed during reproductive examinations of cows.[6]

The virus genome is vertically transmitted via gametes. However, congenital transmission by the transplacental route is rare. Transfer of embryos from BLV-infected cows into uninfected cows has not been associated with transmission of virus. In addition, BLV has not been found in oocytes or embryos obtained from infected cattle. Ova and embryos at the morulae and blastocyst stage have been exposed in vitro to BLV, but the virus could not be detected after the exposed ova or embryos were washed; therefore, it was concluded that it is safe to transfer embryos collected from infected cows, providing the embryos are washed before transfer.[3]

Semen from infected bulls used for artificial insemination is not associated with virus transmission to dams or their progeny. However, in the case of natural breeding, the potential for transmission may exist when heifers are bred by BLV-infected bulls, especially when the genital tract of a heifer is traumatized.[7]

The economic importance of BLV infection is related to financial losses resulting from decreased milk production, death of valuable breeding cattle, condemnation of carcasses at slaughter, increased number of replacements for culled infected cattle, and veterinary costs associated with diagnosis of leukosis. In addition, cattle, semen, and embryos destined for international markets must be negative for BLV.[8]

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