“Trixie’s Lumpy Situation”

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Class of 2022

Clinicopathological Conference

May 14, 2021

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Introduction

Bovine lymphosarcoma (also known as bovine lymphoma) is the most common type of neoplasm of cattle and is one of the main causes of condemnation of adult dairy cows at slaughter. Bovine leukosis encompasses both enzootic bovine leukosis (EBL) and sporadic bovine leukosis (SBL). EBL is caused by infection of the Bovine Leukemia Virus (BLV); SBL is a rare form of lymphosarcoma with no known etiology. While EBL is common, less than 5% of cattle infected develop lymphosarcoma. BLV has been eradicated in many European countries, Australia, and New Zealand through eradication programs. Prevalence of BLV is high in countries such as Argentina, Canada, and the United States of America. A national survey taken in 1996 showed high infection levels in the southeastern US.[2,4,6,7,8]

History and Presentation

Trixie, an 8-year-old dairy mixed breed cow, presented to MSU-CVM Food Animal Department on 05/26/2020. She had been found recumbent for an unknown duration. In April of 2020, Trixie aborted a calf and began losing weight.

Upon presentation to the Food Animal Department, Trixie was down on the trailer. She had a reported body condition score of 3/9. She had pale mucous membranes, and she was breathing heavily. She was approximately 10% dehydrated with injected sclera. A full physical examination was not performed. The owners elected euthanasia by captive bolt followed by intravenous potassium chloride. Trixie was sent to laboratory services for necropsy on 05/27/2020. Trixie presented with a body condition score of 2/9 with moderate post-mortem autolysis. Her skin severely tinted and her sclera were injected.

Pathophysiology

Enzootic bovine leukosis is caused by the Bovine Leukemia Virus (BLV). BLV is a contagious oncogenic retrovirus that infects lymphocytes and is related to the human T-lymphotropic virus type-1 (HTLV-1).[10] The disease caused by BLV results from infection of B-lymphocytes. BLV escapes the immune system through low levels of replication in B-cells. There are 3 main outcomes with BLV: asymptomatic, persistent lymphocytosis, or lymphosarcoma. Most (~70%) infected animals remain persistently infected with no symptoms. Approximately 30% of infected cattle with develop persistent lymphocytosis.[7] Most cattle with persistent lymphocytosis do not display clinical signs, but decreased milk production, immunosuppression, and shortened lifespan have been reported with persistent lymphocytosis.[1] Also, cows with persistent lymphocytosis may be at a greater risk of infecting their calves in utero. Less than 5% of infected cattle will develop lymphosarcoma. Lymphosarcoma is typically seen in older cattle from 4- to 8-years of age. The most common clinical sign with lymphosarcoma is lymphadenopathy of central and/or peripheral lymph nodes. Other common sites affected, and their associated clinical signs, include the uterus (reproductive failure, abortion), abomasum (abdominal pain, melena, abomasal outflow obstruction), heart (arrhythmias, murmurs, heart failure), spine (pelvic limb paresis to paralysis), and retrobulbar area (exposure keratitis and proptosis). Other possible affected organs include the spleen, liver, kidneys, and ureters.[7]

Any material that is blood-contaminated has the potential to infect animals with BLV. BLV is primarily transmitted via provirus-infected lymphocytes in biological material (blood or milk/colostrum) from infected animals to non-infected animals (horizontal transmission). BLV is also transmitted vertically through iatrogenic factors such as tattooing, dehorning, rectal palpation, injections, and blood collection. For these reasons, BLV is more common in dairy

cattle than beef cattle due to their environments and more frequent handling.[7,8] Transplacental infection from dam to fetus through contact with infected blood in utero may occur (~5% of calves).[1] The importance of milk-borne spread is still being studied, but research has shown that transmission via colostrum is not efficient (only ~6-16% efficient when compared to contact transmission). Due to the antibodies contained in the colostrum from BLV-positive dams, calves may be protected from BLV infection because the antibodies are retained for up to 6 months.[12] Insect vectors have also been implicated in BLV transmission, but insect vectors seem to be more important in certain parts of the world than others.[2] Research also suggests that genetics play a role in viral transmission.[5]

Unlike enzootic bovine leukosis, sporadic bovine leukosis (SBL) has no known etiologic agent, and is rare, non-contagious, and non-transmissible. SBL generally occurs in animals less than 3-years of age. SBL is divided into 3 forms of lymphosarcoma: juvenile, thymic, and cutaneous. The juvenile (also known as calf or multicentric) form occurs in animals less than 6 months of age and is characterized by sudden generalized lymphadenopathy with weight loss, depression, and weakness. This lymphosarcoma form is fatal generally within 2-8 weeks of onset. The thymic (or adolescent) form occurs in cattle of 6-24 months of age. The location and size of the tumor generally determines the symptoms, and it typically involves the cervical or intrathoracic thymus or both with cervical swelling. These calves generally present with dyspnea, bloating, jugular distention, tachycardia, anterior edema, and fever. The cutaneous form occurs in cattle 1-3 years of age and is characterized by cutaneous lesions on the neck, back, rump, and thighs. These lesions may regress but often return as generalized lymphosarcoma that carries a fatal prognosis.[3,7,8]

Diagnostics

Trixie did not receive any diagnostics prior to her euthanasia, however, bovine lymphosarcoma would be on her differential list based on signalment, history, clinical signs, and physical examination alone. Both BLV and SBL are routinely diagnosed by history and physical exam alone, but further diagnostics can be utilized. A complete blood count can show a persistent lymphocytosis. Definitive diagnosis of lymphosarcoma is made through fine needle aspirates and cytology along with biopsies of masses. BLV infection can be confirmed through serology (ELISA), virology (PCR), or Agar gel immunodiffusion (AGID). ELISA is the most common test for routine diagnostic usage. ELISA can detect lower numbers of antibodies, however, the presence of antibodies alone does not mean the animal is clinically affected.[4,7] Research suggests that proviral load (PVL) is the best predictor of BLV transmission and disease severity in cattle which can be detected through a qPCR test.[5] While PCR has been shown to detect BLV provirus in blood in the absence of antibodies, PCR requires expensive equipment and experienced technicians which is not practical for most producers.[12] The ELISA is unreliable in calves that have ingested colostrum from BLV-positive dams as these antibodies can last for up to 6 months. AGID is required for most countries as the official import/export test.[4,7,10]

Treatment

There is currently no effective treatment or vaccination available for BLV. As with Trixie, euthanasia is often the outcome in cattle with lymphosarcoma. Prevention is the only treatment option available for EBL. The ideal eradication program is testing and culling, but this is not an economically feasible option for most producers in the USA as the average herd antibody prevalence is approaching 50%. Another option is testing and segregating; this is rarely implemented due to requiring 2 separate operations which requires additional money, time, and

workers.[1,2,7,8,9,12] Management control interventions to prevent iatrogenic transmission should be used; these include using single-use hypodermic needles, single-use OB sleeves, disinfecting instruments between uses, separating BLV-positive cows from calves, feeding calves milk from BLV-negative dams or treated milk, utilizing artificial insemination, and controlling insects.[4,7] These practices are not always effective at decreasing transmission; therefore, other effective methods of control are continuously being sought after.[2]

As stated earlier, PVL may be best predictor of BLV transmission in cattle. One study showed that by using a qPCR test to find and segregate or slaughter cattle with high BLV proviral loads and high lymphocyte counts decreased the incidence and prevalence of BLV in herds within a few years.[1,2] A study showed that major histocompatibility complex (MHC) alleles have been associated with either lower proviral loads and lymphoma resistance or both. MHC class II allele BoLA-DRB3*009:02 has been connected to both lymphoma and PVL resistance. While further research is needed, selecting for this allele may be associated with preventing lymphosarcoma as higher PVL is associated with lymphosarcoma development.[5]

Case Outcome

After being humanely euthanized, Trixie's body was necropsied. Bovine lymphosarcoma was confirmed based on necropsy findings affecting multiple organs, including the heart, uterus, abomasum, and mesenteric lymph nodes. On gross examination, some of the mesenteric lymph nodes were basketball-sized (38 cm x 43 cm x 23 cm) and homogenously pale tan. Also, the abomasal and pulmonary lymph nodes were greatly enlarged and homogenously pale tan. The pericardial sac contained approximately 50-75 milliliters of clear- to yellow-tinged fluid. Both atria were dark purple with large, multifocal thickened pale tan foci that measured up to 2 centimeters in diameter. The right and left ventricular myocardium were dark red brown with

linear pale tan mottling giving a tiger-striped appearance. There were multiple pale tan foci up to 3 cm in diameter present throughout the myocardium of the left and right ventricular walls. The abomasal wall was thickened particularly near the pyloric region measuring up to 2 centimeters. The uterus was diffusely white to tan and thickened approximately to 2 to 3 centimeters wide, and the lumen of the uterus contains scant green tinged fluid. The lymphoma affecting the uterus likely caused Trixie's abortion in April of 2020. The liver was enlarged and pale with a slightly increased reticular pattern.

Conclusion

In conclusion, the most common neoplasm in cattle is lymphosarcoma. Lymphosarcoma in adult cattle is caused by the bovine leukemia virus whereas sporadic lymphosarcoma occurs in younger cattle with no known etiology.[7] Enzootic bovine leukosis is highly prevalent in many countries including Argentina, Canada, and the USA.[2] Less than 5% of cattle infected develop lymphosarcoma with most infected cattle show no symptoms. Persistent lymphocytosis is the most common clinical manifestation of BLV infection. Diagnostic tests to detect BLV in cattle are available, including AGID, ELISA, and PCR. There is currently no effective vaccination with prevention of transmission being the best treatment. Euthanasia is typically the outcome for BLV-infected cattle.[7,8,9,11,12]

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