

What Practitioners Should Understand About Bovine Lymphosarcoma

A. F. La Follette, B.A.*
I. A. Davis, B.S, D.V.M.**

Bovine lymphosarcoma (BLS) is a common neoplasm found in both dairy and beef cattle. It is important for veterinarians, dairy producers and beef producers to gain a thorough understanding of BLS. The first step in understanding BLS is to define the disease. Bovine leukosis, bovine leukemia, bovine lymphoma, and malignant lymphoma are misnomers that add confusion and frustration in understanding the disease process of BLS.

There are currently four distinct forms of BLS: calf form, thymic form, skin form, and adult or bovine leukemia virus (BLV) associated form. In understanding these forms of BLS it is important to know what clinical signs to look for, how to make the diagnosis, the treatment options and recommendations for prevention and control.

Definitions and terminology clarification

The first step in understanding a disease is to define the disease. Bovine lymphosarcoma (BLS) is a disease condition of cattle characterized by tumor formation in the lymph nodes.¹

Often BLS is referred to as bovine leukosis, bovine leukemia, bovine lymphoma and malignant lymphoma. These names are routinely used incorrectly by veterinarians, dairy producers and beef producers. The incorrect use of these names adds confusion and frustration to understanding BLS. There is a distinction to be made. A lymphosarcoma is a malignant lymphoma in which there is neoplastic proliferation of abnormal lymphocytes and immature cells of the series, resulting in the occurrence of multiple enlarged lymph nodes and infiltration of various tissues.² Lymphoma is a general term used to describe various abnormal proliferative neoplastic diseases of lymphoid tissue.² Leukemia is the uncontrolled proliferation of one of the types of white blood cells, or occasionally other forms derived from the reticuloendothelial tissue.² Leukosis is abnormal proliferation of one or more leukopoietic tissues; the term includes myelosis, certain forms of reticuloendotheliosis and lymphadenosis.

* A. F. LaFollete is a 1993 graduate of the Iowa State University College of Veterinary Medicine.

** Dr. I. A. Davis is currently an instructor in the Veterinary Teaching Hospital at Iowa State University.

Leukosis is a broad term and does not specifically identify the disease process, the tissue types, or the cells involved. To say an animal has leukosis could mean nothing more than a "sickness". The term leukemia is descriptive in identifying the disease process as an uncontrolled proliferation of white blood cells, but it does not specify what type of white blood cell is involved. Leukemic syndromes are sometimes associated with certain forms of malignant lymphoma, e.g. lymphosarcoma. Furthermore, an animal with a malignant lymphoma may die without any evidence of leukemia during the later stages of the illness. The definition of lymphosarcoma is descriptive and specifically identifies the disease process, the tissue and the cell type involved as a malignancy of the lymphocytes, resulting in enlarged lymph nodes and metastasis.

Types of bovine lymphosarcoma

Bovine lymphosarcoma (BLS) is currently recognized in four distinct clinicopathologic forms. These are the calf or juvenile form, the thymic or adolescent form, the skin or cutaneous form and the adult or bovine leukemia virus (BLV) associated form.^{1,3,4} There is a possible fifth form of BLS, the non-viral adult form, which is very rare. One source estimates there are only 1.55 cases of the non-viral adult form per 10,000 noninfected cattle.³ This is to say lymphosarcoma is very rare in adult cattle without BLV infection.

Bovine Lymphosarcoma (BLS) is categorized by frequency of occurrence, age of onset, organ systems involved, and the etiologic agent. BLS occurs sporadically in the calf form, thymic

form and skin form. No etiology has been identified for these sporadic forms. The adult form is the most common neoplastic disease in cattle. The adult form is considered to be enzootic in cattle because of the association with the BLV infections.³

Calf form

The calf or juvenile form of BLS occurs as generalized lymphadenopathy in calves less than six months old and is occasionally seen in some fetuses.⁴ The prevalence rate is unknown, occurrence is rare, and dairy breeds are predisposed to developing this form of BLS.³

The calf form clinically presents with a history of depression, weight loss, weakness and sudden onset (within one week). Mucous membranes are pale. Tachycardia, tachypnea, hyperpnea, cough, and harsh respiratory sounds are evident with auscultation. There may also be fever, ruminal tympany, ataxia, and diarrhea.⁵ All clinical signs are dependent on how extensive the neoplastic involvement is.

Clinical pathologic findings for the calf form may include lymphocytosis, microcytic hypochromic anemia, a low hemoglobin (<7 g/100ml), and a low PCV (mid 20's). A bone marrow examination in affected calves may reveal an elevated M/E ratio with massive neoplastic infiltrates.³ There is also a tendency for these calves to have low serum globulin and elevated SGOT.³ This disease is fatal within two to eight weeks after onset of clinical signs.

Thymic form

The thymic or adolescent form of BLS is generally seen in cattle between six months and two years of age. The occurrence is rare. There is a higher prevalence in the beef breeds, particularly in hereford cattle.³

The common clinical presentation of thymic BLS is a poor condition animal with diffuse swelling of the ventral neck. Often there are enlarged prescapular lymph nodes. Clinical signs result from space occupying lesions in the neck or thorax. The thymus is the primary organ involved, though other organs may also be involved. Dysphagia and rumen tympany are commonly seen as a result of impingement on the esophagus. Jugular veins can be distended and nonpulsating. Tachycardia, dyspnea, coughing, and/or respiratory distress may be present.³ These signs are dependent on the amount of neoplastic involvement.

Clinical pathologic findings are generally unremarkable. Anemia is not a consistent feature,

and lymphocytosis is only seen occasionally.⁵ The disease is fatal, these animals often die from bloat.

Skin form

The skin or cutaneous form of BLS is a rare condition seen in cattle from one to three years of age, but is not as age specific as other forms of BLS. The skin form is characterized by the development of tumors beneath the skin surface. Often there is an initial period of one to three months during which cutaneous swellings are found around the anus, vulva, escutcheon, flank and shoulders. Lesions can be raised and ulcerated with necrotic centers. These areas may be painful on palpation. The tumors themselves may resolve or metastasize, producing other lesions such as cardiac insufficiency, ventral edema, elevated pulse and respiration and enlarged lymph nodes.³

Anemia and atypical lymphocytes are common clinical pathologic findings with the skin form.⁴ This disease is fatal if metastasis occurs. On necropsy a variety of organs may be involved. Histopathologic findings for identification is characterized by massive lymphoid infiltration of the skin.

Adult form

The adult or bovine leukemia virus (BLV) associated form is the most common form of bovine lymphosarcoma (BLS). The adult form is typically seen in cattle between four and eight years of age, with a range from two years of age and older. Epidemiologic studies have indicated that the adult form is contagious and is referred to as enzootic among cattle.⁴ The contagious nature is attributed to the discovery of a retrovirus in the lymphocytes of affected cattle. The virus is referred to as the bovine leukemia virus (BLV). BLV is considered to be the etiologic agent for this form of BLS. In the United States, the prevalence of BLV infections range from 10 to 50 percent in dairy cattle and one to 20 percent in beef cattle.⁴ It is important to note that not all cattle with BLV develop BLS. It is now well recognized that only a small percentage (one to five percent) of seropositive BLV cattle develop BLS.⁶

Bovine leukemia virus (BLV) could be considered a misnomer and is often a point of confusion among veterinarians, dairy producers, and beef producers about understanding BLV and its role in BLS. This virus does not produce a true leukemia, thus a more appropriate designation may be the Bovine Leukosis Virus.⁷ As defined earlier, leukosis has a broader definition and does not mislead, as does the word "leukemia", about

the disease process in the adult form of BLS. Adult cattle with BLS may have an elevated peripheral lymphocyte count, but leukemia is not a typical manifestation of lymphosarcoma. Only one third of the BLV infected cattle may develop a persistent lymphocytosis, and this condition can be present for many years in the absence of other clinical signs.⁷ A persistent lymphocytosis can be defined as a benign proliferation of B-lymphocytes.⁷ Again, lymphocytosis is usually not seen with BLS, although the presence of a large number of bizarre, immature, atypical lymphocytes is seen in some cases.

A variety of clinical signs are seen in cattle with the adult form of BLS. Clinical signs are dependent on which body organs neoplastic cells infiltrate and tumors develop. The most notable finding is enlarged peripheral lymph nodes. Internal lymph nodes may be present in the absence of external involvement. The sublumbar and deep inguinal lymph nodes are common sites for tumors. Tumors often invade the gastrointestinal tract, especially the abomasum, causing obstructions or ulcers that lead to anemia, melena, anorexia and weight loss. Diarrhea or constipation are signs of intestinal lymphoid tissue involvement. Tumors in the spinal cord may give rise to neurologic disturbances, such as ataxia, paresis or paralysis. Tumors may invade the bone marrow and crowd out erythropoietic and leukopoietic precursors, creating RBC and WBC abnormalities. Platelet production may be disrupted. Neoplastic involvement of the renal system may produce signs of uremia and renal failure. Reproductive organs may be infiltrated with tumors causing infertility. Clinical signs of cardiac failure are often associated with tumors of the myocardium. Exophthalmus is a frequent occurrence.^{1,3,4}

Diagnosis

In spite of all the clinical and pathologic findings, a definitive diagnosis of BLS requires histopathologic examination of the affected tissues.³ Histopathologic confirmation is needed to rule out granulomatous disease or other types of neoplasm that could produce similar gross tissue changes. Grossly, the tumors associated with BLS are found in encapsulated tissue, usually lymph nodes. The stroma of the tumor everts when cut. The cut tumor tissue is cream colored, moist and friable with little binding structure. The center of the tumors may appear necrotic, whereas peripheral areas are firm.⁴

Another aid in diagnosis of the adult form

of BLS is to identify the BLV infection. Because BLV persists in infected cattle, there is a constant production of antibodies. These antibodies can be detected by a number of serologic tests.

An agar gel immunodiffusion (AGID) test is simple and the most widely used method of BLV antibody detection. This test is inexpensive. Antibody levels are consistently detected two to three months after exposure to BLV. The AGID method may produce some false positives in calves under six months of age, because of persistent colostral antibodies from BLV infected cows.^{6,7}

Enzyme-linked immunosorbant assays (ELISA) are becoming popular. ELISA tests are easy to perform. They are more sensitive than AGID tests.^{6,7}

Radioimmunoassay (RIA) test is the most sensitive. However, RIA is difficult to perform, and is cost prohibitive.⁴

Virus isolation is probably the best method to use in calves under six months of age. The major limitations with virus isolation are the technical difficulty, and the limited number of laboratories performing virus isolation for BLV.⁴

Treatment

There is no curative treatment for cattle with BLS. Both the sporadic and enzootic forms of BLS are progressive and rapidly fatal. The exception is for some of the skin forms of BLS, which are self-resolving.

The BLV infection associated with the adult or enzootic form of BLS is always persistent and no curative pharmaceutical agent can eliminate the infection.

Prevention and control

The sporadic forms of BLS are rare and no etiologic agent has been identified. Because no specific agent is identified, there is little that can be done for prevention and control.

The best way to prevent the adult form of BLS is to prevent BLV infection. BLV spreads primarily by contact that exposes cattle to viral infected lymphocytes. Control and eradication of BLV is best instigated by the reduction of blood transmission through iatrogenic means or physical contact.⁸ Veterinarians can play a significant role in helping to reduce iatrogenic transmission of BLV. The most significant means of doing this is by disinfection of instruments and needles between animals.⁹ A 1:32 sodium hypochlorite solution is one

disinfectant that works well.¹⁰

Rectal palpation is another iatrogenic means of BLV transfer. Routine rectal palpation procedures can result in spread of BLV under conditions found on some dairies, but may not be a major factor in most commercial dairies. Rectal transmission of BLV is related to the frequency of palpation, the amount of rectal mucosa trauma, and the age of the cattle.¹¹ A significant difference is not observed in the rate of seroconversion in heifers and cows in which the same obstetrical sleeve or new sleeves were used for palpation. In commercial dairies, the benefits of changing or washing sleeves between cattle may not be important, but when eradication of BLV is the goal, these measures should be considered.¹¹

BLV can be eradicated from a herd by repeated serologic testing of animals over six months of age, followed by rapid removal of infected cattle. If testing is conducted at three month intervals, the herd is usually BLV free after the second or third test.⁴ Once eradicated, preventive management practices can be instigated to prevent reintroduction of the virus into the herd. The first management tip would be closing the herd and raising all replacement animals. The second tip would be to isolate and test replacement cattle for BLV before allowing them to enter the herd.⁹

If BLV cannot be eradicated from a herd, preventive management practices can be used to prevent BLV transmission to young cattle. This would include removing calves from infected cows prior to nursing and feed these calves colostrum and milk from uninfected cows.^{8,10}

BLV infected animals should be isolated from the rest of the herd. Distance and isolation will help reduce the risk of introduction into naive animals. These isolated animals should eventually be culled in working toward a goal of a BLV free herd.

Conclusion

Veterinarians are the pivot on which a sound understanding of BLS is based. Veterinarians need to be well educated about the four primary forms of BLS and need to be prepared to help dairy and beef producers answer questions related to the disease. Being able to define BLS accurately and point out short comings in misnomer names will be advantageous. These advantages will become evident in recommending preventative and control measures due to a better understanding of the clinical signs and the diagnostic methods used to identify BLS.

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