

SPORADIC LEUKOSIS IN CATTLE SPORADIČNA LEUKOZA KOD GOVEDA

Jože Starič*, Lena Veren Geč, Rok Marzel, Jožica Ježek

Clinic for Reproduction and Large Animals – Section for Ruminants, Veterinary Faculty, University of Ljubljana, Ljubljana, Slovenia

*Correspondence: joze.staric@vf.uni-lj.si



J.S. <https://orcid.org/0000-0002-5156-5277>, R.M. <https://orcid.org/0009-0000-2753-3374>, J.J. <https://orcid.org/0000-0002-3753-5944>

ABSTRACT

Sporadic bovine leukosis (SBL) is a rare neoplastic disease in cattle. It represents a unique challenge for veterinary medicine due to its sporadic occurrence, peculiar clinical presentation and unclear etiology. SBL manifests in four forms: juvenile lymphosarcoma, adult multicentric leukosis, thymic lymphosarcoma and cutaneous lymphosarcoma. In contrast to enzootic bovine leukosis, which is caused by the bovine leukemia virus (BLV), there is no viral link in sporadic cases. They are thought to be caused by multifactorial interactions between genetic predisposition and environmental factors (e.g. carcinogens or other triggers). The diseases are not contagious. The aim of this paper is to review the current knowledge of SBL, focusing on the clinical presentation, diagnostic challenges and potential risk factors. Although sporadic leukosis accounts for a smaller proportion of leukosis cases in cattle compared to BLV-induced leukosis, the impact on affected individuals is severe. SBL must be differentiated from BLV-induced leukosis (absence of BLV antibodies in the blood and absence of BLV in the tissue), which is a reportable disease in the European Union. SBL usually affects younger cattle, but adult animals can also be affected. Adult multicentric leukosis clinically resembles enzootic bovine leukosis with multicentric lymphoproliferative foci and lymphadenopathy, but the affected animals are negative for BLV antibodies. The diseases are progressive and lead to the death of the animals. Diagnostic confirmation of SBL often requires a combination of histopathologic examination, immunohistochemistry and molecular analyses to differentiate it from other neoplastic diseases in cattle. Risk factors such as exposure to certain environmental toxins or genetic susceptibility are thought to play a role in the development of sporadic leukosis. Further research efforts are needed to elucidate the mechanisms underlying the development of SBL and to develop effective prevention and control strategies to control this sporadic but usually lethal disease in cattle population.

Keywords: multicentric leukosis, lymphosarcoma, thymic lymphosarcoma, cutaneous lymphosarcoma, bovine

SAŽETAK

Sporadična leukoza goveda (SBL) je retka neoplastična bolest goveda. Predstavlja jedinstven izazov za veterinu zbog svoje sporadične pojave, osobene kliničke slike i nejasne etiologije. SBL se manifestuje u četiri oblika: juvenilni limfosarkom, multicentrična leukoza odraslih, limfosarkom timusa i kožni limfosarkom. Za razliku od enzootske leukoze goveda, koju izaziva virus govede leukemije (BLV), ne postoji virusna veza u sporadičnim slučajevima. Smatra se da su uzrokovane multifaktorskim interakcijama između genetske predispozicije i faktora životne sredine (npr. kancerogeni ili drugi okidači). Bolesti nisu zarazne. Cilj ovog rada je da se sagledaju dosadašnja znanja o SBL, fokusirajući se na kliničku prezentaciju, dijagnostičke izazove i potencijalne faktore rizika. Iako sporadična leukoza čini manji udeo slučajeva leukoze kod goveda u poređenju sa leukozom izazvanom BLV, uticaj na obolele osobe je ozbiljan. SBL se mora razlikovati od leukoze izazvane BLV (odsustvo BLV antitela u krvi i odsustvo BLV u tkivu), što je

bolest koja se prijavi u Evropskoj uniji. SBL obično pogađa mlađa goveda, ali mogu biti pogođene i odrasle životinje. Multicentrična leukoza odraslih klinički podseća na enzootsku leukozu goveda sa multicentričnim limfoproliferativnim žarištima i limfadenopatijom, ali su obolele životinje negativne na BLV antitela. Bolesti su progresivne i dovode do uginuća životinja. Dijagnostička potvrda SBL često zahteva kombinaciju histopatološkog pregleda, imunohistohemije i molekularne analize da bi se razlikovala od drugih neoplastičnih bolesti goveda. Smatra se da faktori rizika kao što su izloženost određenim toksinima iz životne sredine ili genetska osetljivost igraju ulogu u razvoju sporadične leukoze. Potrebni su dalji istraživački napor da bi se razjasnili mehanizmi koji leže u osnovi razvoja SBL i da se razviju efikasne strategije prevencije i kontrole za kontrolu ove sporadične, ali obično smrtonosne bolesti u populaciji goveda.

Ključne reči: multicentrična leukoza, limfosarkom, multicentric leukosis, lymphosarcoma, timusni limfosarkom, kutani limfosarkom, goveda.

INTRODUCTION

Bovine leukosis or bovine lymphosarcoma (other names are malignant lymphoma and leukemia) is a neoplastic disease of cattle characterized by a progressive and malignant growth of lymphoid tissue in the lymph nodes and other organs. The disease is defined as sporadic or endemic / enzootic according to the frequency of occurrence, the age of the animal in which it occurs, the organ system(s) affected and the causative agent (Hendrick, 2002). It occurs sporadically in calves as generalized lymphadenopathy (calf or juvenile form), thymic leukosis in cattle between 6 months and 2 years of age (thymic or adolescent form) and in 1- to 3-year-old cattle as the cutaneous form. The causative agent of the sporadic forms has not yet been discovered; it appears that they are not infectious in nature. There are approximately 1.55 cases of sporadic forms of leukosis per 10,000 animals that are not infected with the formal bovine leukemia virus (BLV), which was renamed in 2023 into Deltaretrovirus bovine. The most common form of leukosis is enzootic bovine leukosis (EGL) in adult cattle older than 2 years, which is caused by infection with Deltaretrovirus bovine, from the family Retroviridae. It can affect several organ systems simultaneously. Enzootic bovine leukosis is also the most common neoplastic disease in cattle (Hendrick, 2002; Nasir, 2005).

Sporadic lymphosarcomas

Calf or juvenile form

The prevalence of this form is very low and multiple cases in the same herd are very rare (Hendrick, 2002). It occurs uniformly throughout the world.

The cause of the disease is unknown and does not appear to be related to the EGL virus. Experimentally, also the disease cannot be transmitted to healthy calves. There are no differences between the sexes in terms of morbidity, but dairy breeds are said to be more prone to developing the disease (Dubreuil et al., 1998; Frischkorn et al., 2022; Hendrick, 2002).

Calves between 3 and 6 months of age are affected most commonly, but in rare cases it has also occurred in younger calves from 2 weeks of age or in older cattle up to 3 years of age. There are even known cases where sick calves have already been born (Frischkorn et al., 2022; Hendrick, 2002).

The main complaints for seeking veterinary help for sick animals is lethargy, weight loss, weakness despite a good appetite or lymphadenopathy. The disease usually develops rapidly within a week.

Clinical examination shows a generalized bilateral enlargement of the lymph nodes. Rarely, the lymph node enlargement is limited to a specific anatomical region. The enlarged lymph nodes are hard, smooth and painless and may be the size of a hen's egg or even larger. The mucous membranes are usually pale due to anemia. Heart rate and respiratory rate are accelerated. Coughing and abnormal breathing sounds may be present. Rarely, the animals may also have an enlarged liver, increased body temperature, rumen tympany, diarrhea, ataxia or paralysis. The affected animals usually die within 2 to 8 weeks after the first clinical signs appear (Dubreuil et al., 1998; Frischkorn et al., 2022; Hendrick, 2002).

The hematological values of affected animals show microcytic and hypochromic anemia, low hematocrit, thrombocytopenia and leukocytosis due to lymphocytosis. An increased myeloid/erythroid ratio with severe neoplastic infiltration may be seen in the bone marrow. Neoplastic changes can also be

found in various organs, e.g. in the spleen, liver, heart, kidneys, pancreas, uterus and thymus (though less pronounced than in the thymic form). Neoplastic infiltrations may also be found subperiosteally, including in vertebrae, where often comes to pressing on the spinal cord resulting in paresis. Necrotic foci may also be present in the bones (Dubreuil et al., 1998; Frischkorn et al., 2022; Hendrick, 2002).

The disease has also been diagnosed a few times by the faculty of Veterinary faculty.

Thymic or adolescent form

This form of lymphosarcoma is extremely rare. It occurs most frequently in cattle between 6 and 24 months of age, but also rarely in newborn animals and animals up to 4 years of age. Meat breeds are predisposed to the occurrence of this form of the disease (Nasir, 2005). In France, numerous cases of thymic lymphosarcoma have been detected in 5 regions and a large number of affected calves were found to come from the same bull, suggesting that the disease may be hereditary.

The clinical signs are the result of formation that occupy the space on the neck and chest. Most commonly, owners seek veterinary advice because of the swelling in front of the sternum, from the entrance to the chest cavity to the intermandibular space, which is hard and edematous. This often leads to weight loss, rumen tympany (due to pressure on the esophagus) and dysphagia. Generalized lymphadenopathy is rare, but the superficial cervical lymph nodes are often enlarged. The enlarged thymus cannot usually be palpated, but in dissection it is visible in the thoracic cavity. The jugular vein is often tense and does not pulsate. The heartbeat may be less audible. The animal may also be tachycardic, dyspneic, may cough and show signs of respiratory distress (Nasir, 2005).

In some cases, it metastasizes, including to the spinal canal, where it causes compression of the spinal cord (Hendrick, 2002; Nasir, 2005).

The hematological findings are often unremarkable, anemia is present only occasionally and so is lymphocytosis.

It takes 2 to 9 weeks from the diagnosis of the disease to the death of the affected animal, although the disease can cause a deterioration in health months before diagnosis. The disease can quickly lead to death due to acute rumen tympany (Nasir, 2005).

Skin form

This form of lymphosarcoma is also rare, but more prevalent than juvenile and adolescent forms. It occurs in cattle aged 1 to 4 years and is characterized by numerous tumor formations of 1 to 5 cm in diameter on the skin of the neck, back, hips, lower part of the tail, perineum and thighs. From the medical history, we often learn that such changes on the skin may appear for 1 to 3 months, then regress and then reappear. Initially, amber-colored scabs appear on the skin lesions, later gray-white, dry deposits, the hair falls out, then a depression appears in the middle. The lesions may also ulcerate and feel painful. At the beginning they have an elastic consistency, later they are firm-elastic. As a rule, the peripheral lymph nodes are also greatly enlarged and firm. Other clinical signs depend on which organ system is also affected. The animals are often anemic and have lymphocytosis, often with atypical lymphocytes. The disease always ends in death (Klinkon & Černe, 2006; Kureljušić et al., 2019; Loh, 2007; Schweizer et al., 2003).

On pathoanatomical examination, various organs and organ systems can be affected by leukotic changes. The skin changes are grayish in cross-section. The skin is heavily infiltrated with lymphoid cells (Hendrick, 2002; Hugoson, 1970; Klinkon & Černe, 2006; Kureljušić et al., 2019; Loh, 2007; Schweizer et al., 2003). The last time we had a case of cutaneous leukosis at the Clinic for Ruminants was in 2022 (archive of the clinic's patient files).

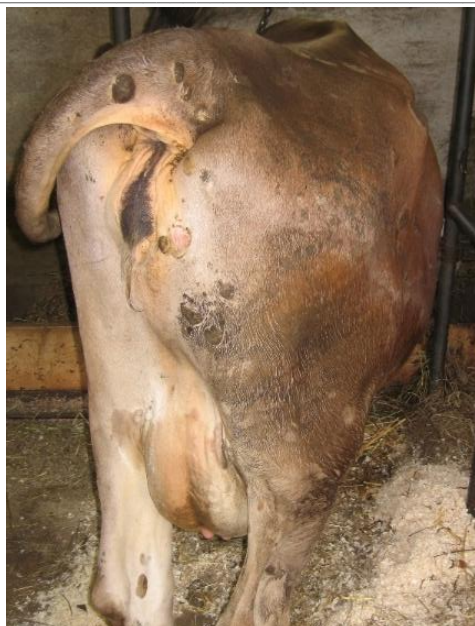


Photo 1: Skin leucosis in Brown cow (note cutaneous nodules, which were firm, hairless and sometimes covered with hemorrhagic crusts) (Photo: J Starič)

Sporadic multicentric lymphosarcoma in adult cattle

Presents similarly as enzootic bovine leukosis, caused by BLV infection. However, in such cases BLV virus cannot be detected by either PCR from blood or affected tissues and the affected animal is also seronegative for BLV antibodies. The disease is sporadic (Freick et al., 2016).

CONCLUSION

Diagnostic confirmation of SBL often requires a combination of histopathologic examination, immunohistochemistry and molecular analyses to differentiate it from other neoplastic diseases in cattle. Cases of SBL also require testing for BLV, to exclude possibility of enzootic bovine leukosis. Especially in countries that are officially free of enzootic bovine leukosis (EBL), such diagnostics is mandatory by regulations. Risk factors such as exposure to certain environmental toxins or genetic susceptibility are thought to play a role in the development of sporadic leukosis. Further research efforts are needed to elucidate the mechanisms underlying the development of SBL and to develop effective prevention and control strategies to control this sporadic but usually lethal disease in cattle population.

LITERATURE

1. Dubreuil P., Lanevski A., Perrone M. A., Desnoyers M. Atypical sporadic lymphosarcoma in a 7-month-old Holstein heifer. *Canadian Veterinary Journal* 1998, 39(7), 431–433.
2. Freick M., Lapko L., Neubert M., Hardt M., Behn H., Passarge O., Schöniger S. Sporadische kutane T-Zell-Leukose mit Beteiligung von Lymphknoten und inneren Organen bei einer Holstein-Kuh. *Tierärztliche Praxis Ausgabe G: Grosstiere – Nutztiere* 2016, 44(1), 39–45. <https://doi.org/10.15653/TPG-150514>
3. Frischkorn M., Fortelny M., Ciurkiewicz M., Krüger J., Jahn-Falk, D. Multicentric B cell lymphoma in an 8-week-old calf. *Tierärztliche Praxis Ausgabe G: Grosstiere – Nutztiere* 2022, 51(2), 109–115. <https://doi.org/10.1055/a-2030-6701>
4. Hendrick S.H. Atypical sporadic bovine leukosis in a beef feedlot heifer. *Canadian Veterinary Journal* 2002, 43(8), 617–619.
5. Hugoson G. Tissue Culture Studies in Bovine Leukosis. *Acta Veterinaria Scandinavica* 1970, 11(1), 103–113. <https://doi.org/10.1186/BF03548007>
6. Klinkon M., Černe M. Cutaneous T-cell lymphoma in a heifer with increased serum lactate dehydrogenase activity. <https://doi.org/10.1111/j.1939-165X.2006.tb00120.x>, 2006.
7. Kureljušić B., Maksimović S., Vujinović S., Savić B., Milićević V., Veljović L., Jezdimirović N., Žutić J. Cutaneous lymphoma in a cow - a case report. *Veterinarski Glasnik* 2019, 73(1), 50–56. <https://doi.org/10.2298/VETGL180904004K>
8. Loh, C. C. (2007). Atypical presentation of cutaneous T-cell lymphosarcoma in a 19-month-old Holstein heifer. *Canadian Veterinary Journal*, 48(3), 309–313.
9. Nasir K. S. Sporadic juvenile thymic lymphoma in a 6-month-old Holstein heifer. *Canadian Veterinary Journal* 2005, 46(9), 831–833.
10. Schweizer G., Hilbe M., Braun U. Clinical, haematological, immunohistochemical and pathological findings in 10 cattle with cutaneous lymphoma. *The Veterinary Record* 2003, 153(17), 525–528. <https://doi.org/10.1136/VR.153.17.525>