Title: Enzootic bovine leucosis (EBL) in a cow

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Clinical History: This 7-year-old Angus cow weighed 1605 lbs on February 18, 2018. On April 1, 2018, the cow was moving slowly and appeared “sucked up”. The weight had dropped to 1490 lbs and the cow developed watery diarrhea. On April 11, 2018, the cow weighed 1177 lbs. Laboratory tests for Clostridium spp., Rotavirus, Giardia, Cryptosporidium, Johne’s disease, and fecal ova and parasites were all negative.

Necropsy Findings: The diaphragm, pericardial sac, and abomasum had varisized, multifocal to coalescing, raised, tan areas.

Gross and Microscopic Images:

Figure 1. Diaphragm. Multifocal to coalescing raised tan lesions.
Figure 2. Pericardium. Marked thickening by neoplastic cells.

Figure 3. Abomasum. Diffuse thickening by neoplastic cells.
Figure 4: Rumen. Neoplastic lymphocytes infiltrate the submucosa and muscular tunics below the mucosal surface. 20X, H&E.

Figure 5: Rumen. Neoplastic cells extend beyond the muscular layer into the surrounding omentum effacing the normal architecture. 20X, H&E.
Figure 6: Neoplastic cells are composed of monomorphic lymphocytes with few mitotic figures. 400X, H&E.

Morphologic Diagnosis (based on the pictures shown):
Diaphragm, pericardium, digestive tract: Lymphoma.

Possible Cause(s):
1. Bovine Leukemia Virus (C Type Retrovirus)
2. Sporadic (Non-Viral): includes calf type, juvenile (thymic) type, and skin type
   a. Calf type: Affects calves less than six months of age; diffuse lymphadenopathy
   b. Juvenile type: Thymic lymphoma in yearlings
   c. Skin type: Affects 2-3 year old cattle with ulcerated plaques on the skin; indolent

Comments: This cow tested positive for Bovine Leukemia Virus (BLV). The condition affecting adult cattle is called enzootic bovine leukosis (EBL), which is the most common neoplastic disease in cattle. Calves are believed to be infected by the virus in their first year of life. Vertical transmission may occur in utero or during delivery, and about 10% of calves born to BLV-infected dams are already infected at birth. The most vulnerable time of transmission is through the ingestion of infected colostrum and/or raw milk either naturally or artificially. Calves infected during the first week of life could play an active role in early propagation of BLV to susceptible animals. Semen has also been discussed as a possible route of transmission, but a recent study by Benitez et al. found that BLV infected bulls that are healthy and aleukemic may not represent a significant risk of BLV transmission during a defined breeding season. Viremia occurs in a small window after infection and prior to antibody formation. Approximately 30% of cattle will experience persistent lymphocytosis as their immune system, specifically the bovine major histocompatibility complex, keeps the virus in check. However, in 3% of cattle, malignant transformation occurs with the peak incidence at 6-8 years of age, as in this case. The cause of malignant transformation is multifactorial, but in 50% of infected cattle, p53 tumor suppressor dysregulation is involved, suggesting a genetic component. As the viral load increases, so does the level of detectable antibody formation. Like most retroviruses, the virus hides in the bone marrow. Dairy cattle are more commonly infected than beef cattle, possibly due to the
fact that direct contact and infected colostrum is believed to be the primary route of infection and is increased during summer months. In North America, an epidemiological study of BLV prevalence in U.S. dairy cattle conducted by the Department of Agriculture’s National Animal Health Monitoring System demonstrated that 83.9% of dairy cattle were BLV-positive at herd level, and 39% of beef herds had at least one BLV-infected animal.

Most neoplastic cells are naïve B cells with rearranged immunoglobulin genes. BLV-induced tumors usually arise from the CD5⁺ IgM⁺ B-cell subpopulation. There are different topographic forms of the BLV associated lymphoma, which include lymph nodes (including but not limited to submandibular, prescapular, supramammary, pelvic nodes); gastroenteric (abomasum); spinal (involving primarily the sublumbar lymph nodes and epidural fat of the lumbar spinal cord); cardiac; uterine; hepatic; splenic; and renal.

There are ten different BLV genotypes worldwide, with each genotype encoding specific amino acid substitutions in both structural and non-structural gene regions. Three genotypes of BLV, namely genotype-1, genotype-4 and genotype-6, are the main across the world. Genotype-1 is the most dominant genotype of BLV and is distributed across almost all continents, including Europe, America, Asia, and Australia. Genotype-1 in particular spread to South and North America, and these continents still have a high prevalence of BLV infection. In the U.S., genotypes 1, 3, and 4 have been detected. The genotypes are spread via animal trade and intercontinental breeding programs.

BLV is significant because cattle with EBL invariably die within months and are not approved for human consumption in some countries. Currently there are no vaccines or treatment, so the only way to control it is to prevent infection. The 30% of cattle that are carriers, referred to as having persistent lymphocytosis, are a constant source of transmission within a herd. Aggressive monitoring of persistent lymphocytosis is a less expensive way to identify carriers than PCR testing; however, little is known about how immune cell reference intervals differ among cattle breeds. Lymphocyte counts in the BLV-free and infected Japanese Black cattle were significantly lower than those in the Holstein cattle, for instance, requiring different diagnostic criteria when assessing lymphocytosis. Of equal concern is evidence that there is a possible causal role of BLV in human breast cancer. BLV has also been found in domestic yaks in China, signifying viral spread between species.

References:

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