Journal of Infectious Diseases and Medicine

Review Article Open Access

Enzootic Bovine Leukosis

Pandey Garima, Agarwal Seema* and Tiwari Aakansha

Department of Veterinary Pathology, College of Veterinary & Animal Sciences, Pantnagar, Uttarakhand, India

Abstract

Enzootic bovine leukosis is a neoplastic disease of dairy cattle and is caused by bovine leukosis virus of R*etroviridae* family. Disease is characterized by proliferation of immune system cells that is B lymphocytes resulting into the condition of B cell lymphosarcoma. The first case of bovine leukosis was reported in 1871 in Eastern Europe. Enzootic bovine leukosis is more prevalent in the areas of America, Australia, Canada and in some European countries. Anorexia, weakness, weight loss, neurological disorders are some of the clinical signs shown by the infected animal. Sheep is the ideal animal model for the experimental inoculation of BLV. Enzootic bovine leukosisis transmitted by contaminated equipments, biting of insects, milk from infected cow. As such no treatment is available, only symptomatic treatment of infected animal is done.

Keywords: Neoplastic disease; Dairy; Cattle; Enzootic bovine leukosisis; Infections; Animals

Introduction

Enzootic bovine leukosis caused by a member of *Retroviridae*, bovine leukemia virus (BLV), is a disease of cattle and water buffaloes. Infected cattle around 30-70% develop persistent lymphocytosis due to the chronic increase in number of circulating B lymphocytes and around 1-5% of infected cattle develop Bcell lymphosarcoma [1]. BLV shows genetic, pathogenicity and sequence similarity with the human T cell leukemia virus (HTLV-1 and HTLV-2). Clinical signs show by infected cattle are digestive disturbances, in appetite, weight loss, weakness or general debility, neurological manifestations, on palpation and rectal examination superficial lymph nodes show enlargement. Organs involved in bovine leukosis are the abomasum, right auricle of the heart, spleen, intestine, liver, kidney, omasum, lung, and uterus. Genetic composition of cattle influences the development of lymphosarcoma and tumor [2]. Prevalence of BLV is more in the areas of Australia, America, Africa and Asia. Presence of virus can be detected in peripheral blood mononuclear cell (PBMC) when cultivated *in-vitro*. Virus as provirus integrate with the infected cell's DNA. Natural body fluids (saliva, milk, nasal and bronchial fluid) also detected for the presence of virus. Natural dissemination of virus occurs through transfer of cells infected with virus. Blood contaminated needles, surgical equipment, gloves used for rectal examinations etc. are responsible for artificial transmission of BLV. Virus is also transmitted mechanically by blood sucking insects especially tabinads. Different diagnostic techniques are used for the detection of virus such as PCR, virus inoculation and serological test. For experimental inoculation, sheep are very susceptible and develop tumours at a younger age than cattle. After experimental infection in deer, rabbits, rats, guinea-pigs, cats, dogs, sheep, rhesus monkeys, chimpanzees, antelopes, pigs, goats and buffaloes, a persistent antibody response can also be detected.

Historical Background

In 1871, the first case of enzootic bovine leukosis was reported in Klaipeda, Lithuania in Eastern Europe where a cow was detected with superficial lymph node hypertrophy and splenomegaly [3]. After reporting of first case, other cases were also reported in the areas indicating that the disease has reached other parts of America. Disease transmission through infectious agent was demonstrated in 1917 [4]. In 1969, presence of virus particles was detected through electron microscopy in lymphocytes of cow suffering with lymphosarcomaby Miller et al. [5] and by applying the Koch postulates, the association between infectious agent and disease was successfully established [6,7]. In 1976, Kettmannshowed BLV particles are the RNA exogenous particle and they also have RNA reverse transcriptase complex and this demonstration led to the virus being the member of oncogenic retroviruses [8].

Prevalence of BLV

Trade of animal products around the world led to the transmission of virus. In European countries, the programmes against the eradication of BLV has been initiated. Belgium, Ireland, Norway has already eradicated the virus and other countries are also on the way of eradication. However, the infection is enzootic in Albania, Bulgaria, Yugoslavia and Poland. America, Australia and Canada are severely affected by the enzootic bovine leukosis. Large percentage of meat herd and dairy animals are affected by the BLV in USA. South African countries has come up with high prevalence of infection. Thus BLV infection has spread all over the world. There is dramatic decrease in the infection rate in Western Europe due to prophylaxes measures based on culling of infected animals from the herd.

Classification and Pathogenesis of Virus

Bovine leukosis virus belongs to *Retroviridae* family, *orthoretrovirinae* subfamily, *Deltaretrovirus* genus which is an exogenous RNA retrovirus responsible for causing enzootic bovine leukosis which is the most common cancer causing disease in cattle worldwide [4-9]. BLV causes chronic and persistent infection in cattle that adversely affect the population of B-lymphocytes [10]. Cattle develop infection after transmission by cellular components of infected bovine blood, by infected cultured cells, or by free virus particles produced in cell culture [3]. Viremia is detected only in first two weeks of infection. Virus can also be detected in intra-follicular

***Corresponding authors:** Agarwal Seema, Department of Veterinary Pathology, College of Veterinary & Animal Sciences, Pantnagar, Uttarakhand, India, Tel: +919756753533; E-mail: seema_patho@rediffmail.com; dr.seemapatho@gmail.com

Received September 18, 2019; **Accepted** November 28, 2019; **Published** December 05, 2019

Citation: Garima P, Seema A, Aakansha T (2019) Enzootic Bovine Leukosis. J Infect Dis Med 4: 137.

and marzin of lymph nodes using immunocytochemistry. Serological response against capsid and envelope proteins develop by the cattle post 2-8 weeks of inoculation. Increase in the B/T lymphocytes shown by the 70% animals infected with the BLV after many years of infection. Among 70% animals, half of animals develop chronic lymphocytosis. The polyclonal proliferation of mature lymphocytes results into increase in the population of lymphocytes and as shown by cytology and cryptology, cells are normal. CD5, CD11b, CD11c lymphocytes are the cells that are affected in the infection. After 1-8 years of infection, appearance of multicentric lymphosarcoma is the rare expression of BLV infection in 1-5% of infected animals. About two-third of animals with tumor have persistent lymphocytosis. The dissemination of virus occurs through two process. In the first process, the virion coupled with the lymphocyte result into the entry of viral single stranded RNA, reverse transcription of genome and ultimately integration of viral genome with the host genome forming provirus. This process is known as infectious cycle. Second process of virus replication involve Tax, regulatory protein of virus which manage cellular proliferation [11].

Clinical Signs and Symptoms

On infection with BLV, animal develop lymphosarcoma. Infected animal become emaciated, loss of appetite, decrease in production, but there is no evidence of fever, enlargement of internal and external lymph node. In 75-90% cases, peripheral lymph node increase in size. Sudden death occurs due to rupture of spleen. Other signs include arrthymia, murmur in heart, blindness, paresis, paralysis, indigestion, ulcers, peritonitis, hematuria, hydronephrosis and intra-abdominal hemorrhage.

BLV Transmission

Natural transmission

In natural cases only zebu, buffaloes and capybaras have been found to be infected. Transmission of virus occur through infected lymphocytes. Another animal become infected with merely 1500 lymphocytes from infected cattle suffering from persistent lymph sarcoma. Transmission of virus is iatrogenic, mainly during the process of dehorning, injections, tattooing and rectal examination. Animals can also acquire infection from bronchial secretion especially when they are house in a crowded place. Sexual transmission of BLV has not been reported. Transmission of virus from mother cattle to calf occur when mother is in the condition of lymphocytosis. Colostrum is the minor source of infection because it contains anti BLV antibodies.

Artificial transmission

For experimental infection with BLV, sheep is mostly used. In 6 months to 7 years of infection sheep develop tumours (lymphosarcoma) after infection with BLV in 90% cases. Because of higher affinity of virus for the ovine cells, the sheep is more susceptible to the infection of bovine leukosis virus. Goats are also susceptible for the infection but less than 3 goats out of 24 develop tumours after infection with BLV [3]. Rabbits develop immunodeficiency disease post 45-763 days of infection. After artificial transmission, antibodies against capsid protein appear in 3 weeks and provirus is form in peripheral blood leukocytes.

Economic Impact of BLV

BLV is not a very serious infectious disease in natural condition. BLV induced tumors cause less economical losses. Early culling of animals from herd occurs because of decrease dairy production of animals with persistent lymphocytosis. Virus also causes immunosupression which predispose the animal to secondary infection and ultimately lead to the death of animal. BLV causes economic losses by reducing animal productivity. Enzootic bovine leukosis leads to the forced culling of infected animal. In raising a dairy cow upto 2 yrs of age when they start producing milk huge amount of expense is occurred. Culling of dairy animal result into loss of money invested on dairy animal. Most insidious economic losses may be associated with subclinical BLV infection. It was reported in the study carried in USA that 3% reduction in milk production was associated with the seropositive cows and the total annual cost of the disease being present in the herd was estimated at $59 per cow [12]. Loss on the potential of cow's production and death of the animal due to lymphosarcoma are the common economic losses caused by BLV [13]. Restrictions are also imposed on the trade of infected animals and their products [14].

The cost of replacing an animal in production, the diagnostic and veterinary care, and the loss of a calf and milk production over about 10 months are indirect economic losses caused by BLV [15].

Diagnosis

Different type of techniques has been developing for the diagnosis of enzootic bovine leukosis. Diagnosis of the infection can be made on the basis of clinical signs such as lymphosarcoma, enlarged lymph node. Conventional serological techniques such as agar gel immunodiffusion (AGID), passive hemagglutination assay (PHA), enzyme-linked immunosorbent assay (ELISA), and radio immunoassay (RIA) have been implemented around the world. A number of PCR methods such as nested PCR, real time PCR, direct blood based PCR have been applied for the detection of infection. Other methods that can be used for detection are the western blotting for the detection of viral proteins, syncytium formation assay and indirect immunofluorescent assay for the detection of BLV antigen.

Differential Diagnosis

Enzootic bovine leukosis can be differentiate with the diseases that develop internal masses such as neoplasia that is carcinoma, melanoma, abscess, and fat necrosis and with the diseases that develop external masses that is *Corynebacterium* pseudotuberculosis that occur rarely in the cattle and tuberculosis caused by *Mycobacterium* tuberculosis and *Mycobacterium* avium that occur rarely in U.S. and more common in other countries.

Treatment

No drug of choice as such available for bovine leukosis, only slaughter and culling of animal is done. Only symptomatic treatment is done such as prednisone.

Prevention and Control

As the prevalence of BLV in Europe and Scandinavia is low so the control programs are effective whereas in USA and Canada prevalence is quite high, therefore control programs are costly. Separate the seropositive cow from the non-infected cow to prevent the transmission of virus. Use the colostrum's from seronegative cow only and always feed calves pasteurized milk and replacer milk. Calving pen of seropositive cow should be separate. Use only BLV negative bulls for service and use insect repellent. Always use sterile needles and equipment's for the dehorning and injections and use of disinfectants.

Conclusion

BLV is the causative agent of enzootic bovine leukosis, which is a neoplastic disease of cattle, buffalo and cypabaras and cause severe economic losses to the dairy and meat industry worldwide. This disease result into B cell lymphosarcoma and persistent lymphocytosis in the uninfected animal. Prevalence of virus is more in America and European countries so preventive measures should be taken to check the transmission of BLV. Vaccination against the EBL is under trail. For reducing the incidence of EBL in the herd, different diagnostics approaches should be developing. Development of therapeutics against the disease is the area where more emphasis should be laid.

References

1. Burny A, Cleuter Y, Kettmann R, Mammerickx M, Marbaix G, et al. (1988) Bovine leukemia facts and hypothesis derived from the study of an infectious cancer. Adv Vet Sci Comp Med 32: 149-170.
2. Gillet N, Florins A, Boxus M, Burteau C, Nigro A, et al. (2007) Mechanisms of leukemogenesis induced by bovine leukemia virus: prospects for novel anti-retroviral therapies in human. Retrovirology 4: 18.
3. Burny A, Bruck C, Chantrenne H (1980) Bovine leukemia virus. Molecular biology and epidemiology. Raven press. New York.
4. Schwartz I, Levy D (1994) Pathobiology of bovine leukemia virus. Vet Res 25: 521-536.
5. Miller JM, Miller LD, Olson C, Gillette KG (1969) Virus like particles phytohemagglutinin, stimulated lymphocyte cultures with reference to bovine lymphosarcoma. J Ntl Cancer Inst 43: 1297-1305.
6. Olson C, Hoss HE, Miller JM, Baumgartener LE (1973) Evidence of bovine C-type (leukemia) virus in dairy cattle. J Am Vet Med Assoc 163: 355-357.
7. Olson C (1974) Bovine lymphosarcoma (leukemia) a synopsis. J Am Vet Med Assoc 165: 630-632.
8. Kettmann R, Portetelle D, Mammerickx M (1976) Bovine leukemia virus: an exogenous oncogenic virus. Proc Natl Acad Sci USA 73: 1014-1018.
9. Moratorio G, Fischer S, Bianchi S, Tomé L, Rama G, et al. (2013) A detailed molecular analysis of complete Bovine Leukemia Virus genomes isolated from B-cell lymphosarcomas. Vet Res 44: 19.
10. Kettmann R, Cleuter Y, Mammerickx M, Meunier-Rotival M, Bernardi G, et al. (1980) Genomic integration of bovine leukemia provirus: comparison of persistent lymphocytosis with lymph node tumor form of enzootic. Proct Natl Acad Sci USA 77: 2577-2581.
11. Villalobos-Cortés A (2107) Enzootic bovine leukosis and the risk to human health. Afr J Biotechnol 16: 763-770.
12. https://vet360.vetlink.co.za/disease-overview-enzootic-bovine-leukosis/
13. Juliarena MA, Barrios CN, Lützelschwab CM, Esteban EN, Gutiérrez SE (2017) Bovine leukemia virus: current perspectives. Dovepress 9: 13-26.
14. Bartlett PC, Sordillo LM, Byrem TM, Norby B, Grooms DL, et al. (2014) Options for the control of bovine leukemia virus in dairy cattle. J Am Vet Med Assoc 244: 914-922.
15. Rhodes JK, Pelzer KD, Johnson YJ (2003) Economic implications of bovine leukemia virus infection in mid-Atlantic dairy herds. J Am Vet Med Assoc 223: 346–352.