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Review Paper

A Review: Lumpy Skin Disease in Cattle

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ABSTRACT

Lumpy skin disease (LSD) is one of the most economically valuable transboundary and OIE-listed diseases caused by Capripoxvirus in the family Poxviridae. LSD should always be included in the differential diagnosis when cattle exhibit tiny nodules development in the head, neck, udder, rump, perineum, and leg area and elevated body temperature, respiration, and salivation. The economic potential of these diseases is of significant concern, provided that they threaten international trade and could be used as economic bioterrorism agents. Because of the scarcity of reliable vaccinations and the widespread poverty in rural areas, capripoxviruses appear to be spreading more widely. The best treatment for reducing the risk factors for the disease could be strict quarantine, vector control, and prophylactic vaccination. The goal of the current study is to give the information that is currently available on the disease's various aspects, including its clinicopathology, method of transmission, possible treatments, and diagnostic procedures.

Keywords: Nodule's development, Transboundary disease, Cattle

Lumpy skin disease (LSD) is an emerging viral disease of cattle caused by a double-stranded DNA virus belonging to the Capripoxvirus genus of the family Poxviridae (Gupta *et al*. 2020). LSD is among the most economically valuable transboundary and OIE listed diseases (Seyoum and Teshome, 2017). In the past 70 years, the virus that causes lumpy skin disease has migrated north and south from its sub-Saharan African origins (Woods, 1988). It can be spread by direct contact, contaminated food and water, iatrogenic methods, arthropod vectors (female Aedes aegypti mosquitoes), and other mechanisms. LSD is a disease that has a significant economic impact since it causes temporary or permanent loss of milk production, infertility or even sterility in bulls, abortion of pregnant cows, decreased weight growth, and irreversible damage to hides (Leliso *et al.* 2021). The diagnosis of LSD is based on the history, clinical features, and occurrence of comparable cases in other places (Feyisa, 2018).

PATHOGENESIS

In the generalized type of LSDV infection, viral replication, viremia, and fever are followed by localization of the virus in the skin and the formation of nodules (Constable *et al.* 2017). In studies, the following events were noted following viral inoculation (intradermal or subcutaneous).

- 4 to 7 days post-infection (DPI): localized swelling varying from 1–3 cm nodules or plaques at the site of inoculation and 25% of skin surface affected.
- 6 to 18 DPI: viremia and shedding of the virus via oral and nasal discharge.
- 7 to 19 DPI: enlarge of regional lymph node and development of generalized skin nodules.

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- 39 days after fever: presence of virus in saliva.
- 42 days after fever: presence of virus in semen (Coetzer, 2004).

Virus replication Intracellular in fibroblasts, macrophages, pericytes endothelial and blood vessels and lymph vessels resulted vasculitis and lymphangitis in affected tissues (Coetzer, 2004). Thrombosis and infraction may happen in severely infected cases. Lactating cows and underweight animals are particularly vulnerable to natural infections because young calves' humoral immunity is impaired (Babiuk, Bowden, Boyle *et al.* 2008). Animals that had been naturally infected by the virus but had recovered showed lifetime immunity. Due to developed maternal antibodies, calves born to their diseased cow are resistant to disease for around six months (Tuppurainen *et al.* 2005).

CLINICAL SIGN

For naturally occurring cases, the incubation time for LSD is 2 to 5 weeks, however for artificially infected calves, it is 1 to 2 weeks. LSD has two different classifications: moderate and severe. The number of lumps (nodules), the dosage of the inoculum, the host's susceptibility, and the density of the insect population are used to classify it. It is characterised by fever, increased nasal discharge, watery eyes, and skin nodules that can be seen on the head, neck, udder, rump, perineum, and leg area (Pandeya *et al*. 2021).

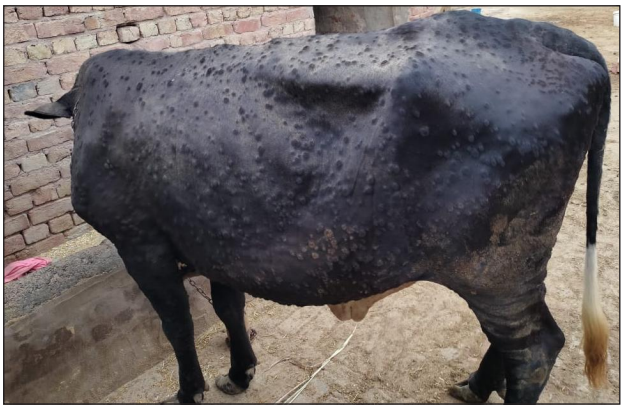

Fig. 1: Characteristic LSD nodular lesion indicating severity: Lesion covering the whole body in severe form

Additionally, infected cows and bulls can become infertile temporarily or permanently. The respiratory and digestive systems both exhibit lesions. Infected cattle may experience substantial morbidity but low death as a result of the disease. When compared to other conditions, LSD may be distinguished from urticaria, streptotrichosis, ringworm, hypoderma bovis infection, photosensitization, bovine papular stomatitis, foot-and-mouth disease, bovine viral diarrhoea, and malignant catarrhal fever (Al-Salihi, 2014).

PATHOLOGY

(a) Gross pathological lesion

Skin nodules that are uniform in size, firm, round, and elevated are found over the entire body (Weiss, 1968). Some nodules may fuse into irregular shapes and circumscribed plaques (Babiuk, 2018). In a few cases, lymphadenopathy was seen. Skin nodules may exhibit pathognomonic eosinophilic intracytoplasmic inclusion bodies upon histological investigation. Additionally, the lesions produce an ulcer that gradually heals via granulation tissue since they are separated from the necrotic epithelium far from the healthy tissue (Al-Salihi, 2014).

(b) Histopathological lesion

Pathognomonic eosinophilic intracytoplasmic inclusion bodies may be seen under a microscope during the histological investigation of skin nodules. There is also an infiltration of inflammatory cells such eosinophils, lymphocytes, and macrophages. Microscopically, inclusion bodies revealed keratinocytes, macrophages, endothelial cells, and pericytes, which are linked to the ballooning and degeneration of the spinosum cells layer. Additionally, in certain situations, subcutaneous muscles may have significant coagulative necrosis and extensive vasculitis (Constable *et al.* 2017) (Sevik *et al.* 2016).

DIAGNOSIS

The history, clinical signs and symptoms, and laboratory results can all be used to confirm the diagnosis of LSD. Recently, ELISA kits were available in the market. To further verify the case utilising real-time PCR or traditional PCR procedures (Orlova *et al.* 2007) (Tuppurainen *et al*. 2005) (Balinsky *et al*. 2008) (Bowden *et al.* 2008). Furthermore, as indicated in Table 1, LSDV has

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Table 1: Different Technique of LSD diagnosis

Purposes	Technique	Epidemiological investigation	Screening prior to movement	Contribute to eradication	Confirmation in clinical cases	Prevalence of infection surveillance	Immune status post vaccination
Agent identification	Virus isolation	+	++	+	+++	+	-
	Electron microscopy/IFAT	-	-	-	+	-	-
	PCR	++	+++	++	+++	+	-
Detection of immune response	Virus Neutralization	++	++	++	++	++	++
	Indirect fluorescent antibody test	+	+	+	+	+	+

Note: *+++ = recommended method; ++ = suitable method; + = may be used in some situations, but cost, reliability, or other factors severely limits its application; – =not appropriate for this purpose. PCR=polymerase chain reaction; VN=virus neutralization; IFAT=indirect fluorescent antibody test, adapted from OIE.*

Fig. 2: Pock lesion of LSDV on CAM scattered white foci. numerous, small

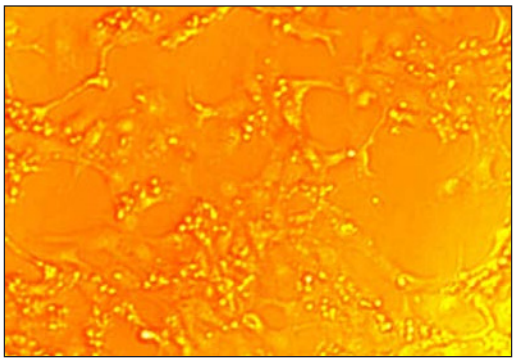


Fig. 3: Characteristic CPE of LSD in the form of clusters of cells rounding, cell aggregations and vacuoles then cell beginning of detachment

been detected using electron microscopy, viral isolation, virus neutralisation, and serological methods (OIE, 2018). Electron microscopy analysis and serum or virus neutralisation tests, respectively, are the gold standard techniques for detecting viral antigen and antibody (Tuppurainen *et al.* 2011). In an experimental investigation, Babiuk, Bowden, Parkyn *et al.* (2008) confirmed immunohistochemical identification of LSDV antigen. The western blot test is costly and challenging to perform despite its sensitivity and specificity (OIE, 2018).

Some labortary test used in labortary diagnosis of LSD, that are given below:

Isolation of the virus

It is necessary to isolate and identify the virus in order to confirm lumpy skindisease in a new location. Before the development of neutralizing antibodies, samples for viral isolation should be obtained during the first week after the emergence of clinical symptoms (Davies, 1991) (Davies *et al.* 1971). Early lesions (those without necrosis) on the skin can be biopsied to obtain samples for viral isolation and electron microscopy. Additionally, during the viraemic stage of LSD, blood samples taken into EDTA or heparin can be used to isolate the LSD virus from buffy coat. At least three different animals should be used for the samples. For viral isolation, samples aspirated from swollen lymph nodes can also be employed. LSD viral replicates in tissue cultures obtained from bovine, ovine, or caprine origin.

The most vulnerable cells are thought to be lamb testis (LT) cells or bovine dermis cells (primary or secondary culture). The African green monkey kidney (Vero) cells and the chorioallantoic membrane of embryonated chicken eggs have both been adapted to support the growth of LSD

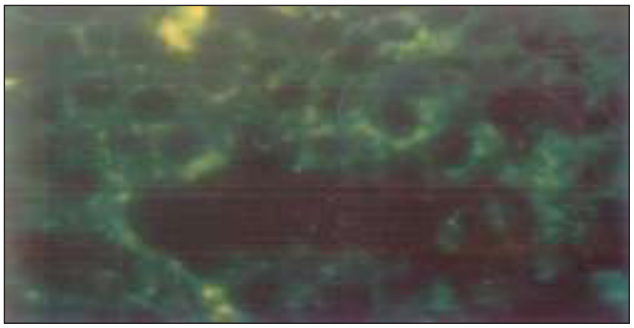
capripoxvirus, which is not advised for primary isolation (OIE Terrestrial Manual, 2010).

Electron microscopy

Within a few hours after receiving the samples, a transmission electron microscopy (TEM) diagnosis of LSD can be performed. TEM evidence of the virus in biopsy tissues from affected skin or mucous membranes that were negatively stained. The average dimension of mature capripox virions is 320 x 260 nm, and they have a more oval form and bigger lateral bodies than orthopox virions (OIE Terrestrial Manual, 2010).

Fluorescent antibody tests

Fluorescent antibody assays can also be used to detect the capripoxvirus antigen on contaminated tissue culture slides or cover slips.



Source: *El-Nahas et al. (2011)*

Fig. 4: The specific intracytoplasmic yellowish green fluorescent granules

Agar gel immunodiffusion

The precipitating antigen of capripoxvirus has been detected using an agar gel immunodiffusion (AGID) assay, although same antigen is also present in parapoxvirus, that is a disadvantage.

Enzyme-linked immunosorbent assay

It is created by employing expressed recombinant antigen to create P32 monospecific polyclonal antiserum and the synthesis of monoclonal antibodies (MAbs) (Carn *et al.* 1994).

Capripoxviruses have been more sensitively detected using the polymerase chain reaction (PCR) and the loop-mediated isothermal amplification (LAMP) test (Bowden *et al.* 2009) (Balinsky *et al.* 2008).

Serology

Frozen sera from both acute and convalescent animals are used. Both the indirect fluorescent antibody test (cross-reaction with parapoxviruses) and viral neutralization (cross responds with all capripoxviruses) are frequently used. The expressed structural P32 protein has been used in the development of an enzyme-linked immunosorbent test for the detection of antibodies against the capripox virus (Carn *et al.* 1994) (Heine *et al.* 1999). Agar gel immunodiffusion test (This test may give false-positive reactions due to cross reaction with bovine papular stomatitis virus and pseudo cowpox virus). Although the test is costly and challenging to perform, Western blot analysis offers a sensitive and specific approach for the identification of antibodies to capripoxvirus structural proteins.

TREATMENT

There is no specific treatment available for LSD. The treatment of LSD is only symptomatic and targeted at preventing secondary bacterial complications using antimicrobial therapy (Abutarbush *et al.* 2015). Besides, that anti-inflammatory drug to be given to alleviate the pain and to enhance its appetite. Supportive therapy and anti-septic solutions also used for treatment (Salib and Osman, 2011).

PREVENTION AND CONTROL

The four major ways for managing and preventing LSD are vaccination, slaughter campaigns, movement restriction (quarantine), and management strategies. The disease can be effectively controlled by immunising susceptible animals. The capripoxvirus family is known to offer cross-protection. Therefore, cattle can be protected against LSD infection using both homologous (Neethling LSDV strain) and heterologous (sheep pox or goat pox virus) live attenuated vaccines (OIE, 2013). The most effective vaccines are made from the Neethling strain virus (Ayelet *et al.* 2014). A clinical diagnosis must also be quickly confirmed in order to implement eradication measures like quarantine, slaughtering of affected and infected animals, proper carcass disposal, cleaning and disinfecting of the area, and insect control as soon as possible during the eruption (Constable *et al.* 2016) (Tuppurainen *et al.* 2005).

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CONCLUSION

LSD was a newly emerging disease. Although LSD disease mortality is low, it significantly affects the economy due to reduced milk production, infertility, recumbency, and expensive long-term therapy. Therefore, to prevent future spread, it is strongly advised that endemic regions adopt precise and timely diagnosis, strict quarantine, biosecurity, immunization, and LSDV testing of bulls used for breeding.

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