



A Brief Review on Vesicular Stomatitis

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Abstract

Vesicular stomatitis (VS), though exotic to India, the most common zoonotic vesicular disease affecting different animal species, is due to a bullet-shaped Vesicular stomatitis virus (VSV) that belongs to the *Vesiculovirus* genus in the *Rhabdoviridae* family. The disease looks clinically very similar to four different diseases, *e.g.*, foot and mouth disease, vesicular exanthema of swine, swine vesicular disease and disease caused by Seneca Valley virus. Cattle, horse and pig are most severely affected. Humans get in frequently infected with VS through handling affected animals and exhibits flu-like symptoms. Though various ways of VSV transmission have been reported, transmission by direct contacts and vector are observed under natural field situations. Indirect sandwich ELISA, multiplex RT-PCR and real-time PCR platforms are efficient for concomitant detection of VSV and other look-a-like vesicular diseases. Despite the availability of vaccines against VSV, vector control and elimination are of paramount importance along with proper biosecurity measures however, should be in place for effective prevention and control of the disease.

Keywords: Cattle, Horse, Pig, Vesicular stomatitis virus

Introduction

Vesicular stomatitis (VS), a common zoonotic vesicular disease in the Americas, considered exotic for India, is an economically important viral ailment of cattle, horse and pig. Even though the disease is not so fatal, its devastating economic impacts on the livestock productivity can be crippling owing to associated production losses and restrictions imposed on animal movement. The monetary loss from one VS outbreak in USA was calculated at \$ 100 to \$ 200 cow⁻¹ (Hayek *et al.*, 1998). Further, being clinically sharing alike features to foot and mouth disease (FMD), any incidence of VS sets a wake-up alarm as the US has been free from FMD since 1929. In view of recent incursions of African swine fever (ASF) and lumpy skin disease (LSD), which were earlier exotic to India, awareness on other such diseases is of paramount importance in public.

VS earlier occupied a position in the List A World Organization for Animal Health (OIE) disease indicating its mandatory international reporting requirements. Afterwards, owing to its mild and self-limiting nature and unlikely chance of cross-border spread between countries through animal trade, VS has been de-listed by the OIE as a reportable disease;

however, it has been categorized as one of the more than 100 'listed diseases' as per the new OIE scheme. The disease is clinically very similar to FMD, vesicular exanthema of swine (VES), swine vesicular disease (SVD) and disease caused by Seneca Valley virus (SVV); hence, each incidence ought to move through a meticulous investigation.

Causative Agent

Vesicular stomatitis virus (VSV) is the etiological agent of Vesicular stomatitis (VS). Despite being reported since the 1800s, the virus was first isolated in 1925. VSV is enveloped, non-segmented, large bullet-shaped (65-185 nm) arthropod-borne virus in the *Vesiculovirus* genus in the *Rhabdoviridae* family (Rose and Whitt, 2001). The genome is composed of a negative sense single-stranded RNA of 11,161 nucleotides encoding 5 major proteins, *e.g.*, matrix protein (M), glycoprotein (G), nucleocapsid or ribonucleoprotein (N), phosphoprotein (P) and large protein or polymerase (L). Two serotypes of VSV are reported, *e.g.*, VSV New Jersey virus (VSV-NJ) and VSV Indiana virus (VSV-IND) each again categorized into serological groups/ subtypes as per the geographic origin. Though both serotypes are virulent in domestic animals, VSV-IND has never been found involved

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with clinical disease in pig. Three distinct serogroups/subtypes of Indiana serotype are described, e.g., classical (IND-1) representing the classic Indiana strains, Cocal virus (COCV) (Indiana 2 subtype or IND-2) first recovered from mites from rice rats in Trinidad during 1961 and Alagoas virus (VSAV) (Indiana 3 subtype or IND-3) first isolation done from a Brazilian mule of Alagoas during 1964. Besides these, other vesiculoviruses are there with hardly any importance in natural outbreaks in animals. These include Brazilian Piry virus, Indian Chandipura virus, Iranian Isfahan virus, Maraba, Porton-S, Jurona, Calchaqui, Carajas and Perinet.

Susceptible Species

VSV can affect cattle, buffalo, sheep, goats, camel, horse and pig. Cattle, horse and pig are most severely affected. Central America, Mexico and north part of South America suffer from the endemic VSV, while northern Mexico and the United States report with less frequency. The last record of VSV-NJ infection in the US was reported in pig in 1968, while further spontaneous occurrence of the same in swine has never been reported there.

Zoonotic Potential

VS is zoonotic and human coming in direct contact with infected animals can pick up infection exhibiting flu-like symptoms of fever, headache, fatigue and muscle pain for few days and vesicular lesions within 1-2 days, but the disease is never fatal in human rather mild and self-limiting.

Cleaning and Disinfection

Sunlight readily inactivates VSV and the similar effect is achieved also from intense UV irradiation or heat at 56 °C for half an hour. The virus is sensitive to 1% sodium hypochlorite (NaOCl or bleach), 2% glutaraldehyde [(CH₂)₃(CHO)₂], 2% sodium carbonate (Na₂CO₃), chlorine dioxide (ClO₂), 1% formalin (CH₂O), 70% ethanol (C₂H₆O), 4% sodium hydroxide (NaOH), 2% iodophore disinfectants. The agent shows stability at a pH range of 4-10.

Morbidity and Mortality

Though morbidity rate in VS follows a wide variation between 5% and 70%, it can reach even up to 90-96%. Mortality due to VS is uncommon. Adult animals are mostly affected. Most of the outbreaks (80%) in USA are attributed to the New Jersey serotype, while Indiana 1 is the cause for others. Only 10-15% of animals exhibit clinical signs and most of them recover from the disease within two weeks.

Transmission

Insect vector transmission and direct contact have been described under natural conditions. Transmission occurs through transcutaneous/ mucosal routes and largely via arthropod vectors, e.g., sand flies (*Phlebotomus* sp. and *Lutzomyia* sp.), black flies (*Simuliidae*) and mosquitoes (*Aedes* sp.). Epithelial tissues are the common predilection sites of the virus while blood or semen transmission has never been evident. The seasonality has an influence upon the occurrence of the disease. Outbreaks of vesicular stomatitis occur during predominance of vector activity. In animal-to-animal contact studies, naïve pigs became infected when housed with pigs inoculated with VSNJV intradermally

on the snout. It is also demonstrated that for animal-to-animal contact transmission formation of prominent vesicular lesions are necessary. VSV Indiana 1 serotype has been detected in sand flies (Order Diptera: Psychodidae), hematophagous insects such as black flies (*Simuliidae*), mosquitoes (*Culicidae*) and *Culicoides* (*Ceratopogonidae*).

In outbreak situation, VSV rapidly spreads within flocks of susceptible animals through direct contacts and fomites. VSV-affected animals secrete saliva profusely releasing large quantity of virus (Hanson and Brandly, 1957). Insects as mechanical vectors or biological vectors play a crucial role in spread/ dissemination of the virus.

Mechanical Vector Transmission

Insects follow mechanical transmission by transporting virus physically characterized by low insect specificity with no incubation period. During various epizootics, VSV was recovered from non-blood sucking insects like houseflies and eye gnats.

Biological Vector Transmission

On contrary to mechanical transmission, biological transmission is characterized by a higher degree of insect specificity and an additional extrinsic incubation period during which VSV profusely proliferates prior reaching to organs like salivary glands and eggs. Sand flies have been the earliest and most frequent insect species involved in natural infection and were reported to be capable of transovarial transmission.

Pathology and Symptomatology

Vesicular stomatitis is a self-limiting ailment and most of the animals recover with healing lesions in two weeks. The incubation period for VSV is variable but usually vesicles are visible within 24-72 h after virus inoculation. In ruminants and pigs, the symptoms of VS resemble those of FMD characterized by initial blanched and raised vesiculation progressing to erosive ulcerations on the tongue, muzzle, palate, gum, lips, snout (in pig), occasionally teats, prepuce, interdigital space and coronary band. Little interest in food and weight loss may occur in some animals due to vesicle-induced pain and discomfort. Feet and/or snout are the common sites of lesions in pigs. Oral lesions lead to excess salivation and inappetence while lesions around coronary band lead to lameness. Lameness is typically manifested in pig, while salivation and drooling are often featured in horse and cattle. Because of clinical and pathological similarity to FMD in cattle and pigs, a clear and precise investigation should follow in all suspected VS cases. Furthermore, concomitant VSV and FMDV infections have been experimentally reproduced as well as naturally reported in cattle. SVD and VES are the two important diseases in pigs that must be considered for a differential diagnosis from VS. Clinical signs of VS are not grossly differentiated from symptoms and lesions inflicted by FMDV, VESV, SVDV and SVV. When three species swine, bovine and equine are contemporaneously affected in a region, VS should be gained suspicion as equines are refractory to FMDV. On contrary, when infection is limited only to cattle and pig, FMD should be kept in the mind during investigation. Both cattle and

pigs have been reported to be infected with SVV. SVD as well as VES may be taken into consideration for differential diagnosis when only pigs are affected. Histologically, mucosal vesiculations appear in VSV infection and resultant rupture creates cavitations containing cellular exudates, lysis of epithelial cell and edema characterized by inflammatory cells infiltration in the affected portions.

Samples and Diagnosis

Vesicular/ blister fluid, epithelium of unruptured blisters and swabs of fluid from ruptured vesicles are the preferred specimens. Serum is the sample for antibody detection. Oropharyngeal fluid (OPF) from cattle and swab from throat of pigs should be collected for recovery of virus especially when there is lack of epithelial tissue in vesicular lesions. Naso-pharyngeal swabs are helpful to make an early diagnosis prior to initiation of clinical signs using RT-PCR. Diagnosis of VSV is made by CFT, electron microscopy, cell culture isolation of virus and ELISA. One-step multiplex RT-PCR tests are more preferred to make a fast and concomitant diagnosis of VSV and other look-a-like vesicular diseases. Baby hamster kidney cells (BHK-21), African green monkey kidney (VERO) and pig kidney (IBRS-2) cell cultures are used for VSV isolation and propagation.

Prevention and Control

As a precautionary measure, ICAR-NIFMD ensures VSV screening of suspected clinical samples found negative for FMDV. Undoubtedly, vaccines are effective for viral diseases and accordingly, inactivated and recombinant VSV vaccines have been developed for VS for use in endemic countries. However, aggressive insect/ vector control should be prioritized with use of biologically safe insect repellants such as permethrin. Strict adaptation of biosecurity measures can prevent virus spread through infected animals, workers/ animal attendants or fomites. Spray of insecticides and treated ear tags/ IDs are to be preferred as pastured domestic stocks are frequently affected. A minimum of 14 days quarantine is applicable to all VS-susceptible species present in the infected areas/ boundary without allowing

any further dynamics/ movement. Affected animals should be isolated from the apparently healthy animals in order to reduce within-herd spread.

Conclusion

The epidemiology of VSV is complex because of wide host range, multiple routes of transmission, clinical variation as per site of infection and involvement of a diverse range of vector species. Vesicular stomatitis (VS) is a common zoonotic livestock vesicular ailment that is grossly similar to disease caused by FMDV, VESV, SVDV and SVV. Bovine, equine and porcine are the species most severely affected. Humans sometimes acquire infection from VSV-affected animals showing flu-like signs. Under natural conditions, insect vector transmission and direct contacts have been described for VSV transmission. The indirect sandwich ELISA, one-step multiplex RT-PCR tests are popular for fast and concomitant detection of VSV and other similar looking vesicular infections. Even though vaccines are available, insect control and biosecurity measures should be practiced for effective control and prevention of virus spread. Even though India is free from vesicular stomatitis, a prior preparedness and diagnostic capability is required for any emergent situation arising out of any such suspicion.

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