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Pathology of Ganjam virus disease in small ruminants

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Abstract

Ganjam virus disease is a tick-borne infection caused by Ganjam virus, a member of genus *Nairovirus* of family *Bunyaviridae*. Ganjam virus is widely prevalent in Asian countries including India. The virus mainly affects the exotic and crossbred sheep and goats causing high morbidity and mortality. The virus has public health significance, although it causes only a mild influenza like illness in human which usually disappears after three days. Clinical signs comprise anorexia, biphasic fever, conjunctivitis, serosanguineous nasal discharge and dried crust present around the nostrils. Grossly, petechial to ecchymotic hemorrhages are present on the serous and mucous membrane of various visceral organs. Microscopically, there is increase thickness of the wall of caecum and colon with streaks of congestion on the mucosal folds of rectum. Hence, it is advisable to adopt preventive measures such as dipping or spraying of the animal by acaricides and adopting the sanitary prophylaxis to help combating this infection.

Keywords: Asian countries, Ganjam virus, Goats, Sheep

Introduction

In the present scenario, due to climatic and human habitat occupation changes; the impact of tick borne viral infection is increasing. One of the highly pathogenic, tick-borne viral infections of small ruminants (sheep and goats) is called Ganjam virus (GANV) infection in India. It is also reported from African countries as a variant is called Nairobi sheep disease virus. Despite these two names, Ganjam virus and Nairobi sheep disease virus are now considered to be the same virus and responsible for several outbreaks of disease^[18]

Nairobi sheep disease virus takes its name from where it was originally isolated, Nairobi, Kenya in 1910. For the rest of the 20th Century, it was believed that Nairobi sheep disease (NSD) was endemic to East Africa. Ganjam virus is recognized as an Asian variant of Nairobi sheep disease virus and was named after the location of isolation, Ganjam city in Orissa, India^[3]. This Ganjam virus disease (GANVD) is widely prevalent in Asian countries (i.e.) India, Pakistan, China and Sri Lanka etc. This disease is on the list of diseases, notifiable to the World Organization for Animal Health^[2].

It is a non-contagious tick borne infection, characterized by biphasic fever, acute hemorrhagic gastroenteritis, profuse fetid diarrhea and abortion. The disease has high morbidity and mortality rates, reported up to 90% in susceptible population^[23]. It can cause a similar clinical picture with other important pathogenic diseases which are endemic in India and its neighboring countries such as Peste des petits ruminants (PPR), Rift valley fever, Salmonellosis, Heart-water disease, Coccidiosis, and some toxicity like Arsenic poisoning etc.^[19]. Therefore, if this disease once occurs it may deteriorate the health and production of animals and socio-economic status of the farmers and country^[1]. GANV is capable of human infection, causing only a mild influenza like illness, those affected, all recovered. Neither GANV nor NSDV are considered a significant threat to public health, however they are to be studied at biological safety level 3 diseases^[24].

Aetiology

Classification of virus: According to the International Committee on the Taxonomy of viruses, this virus belongs to the Family- *Bunyaviridae* and Genus – *Nairovirus*^[16].

Morphology of virus: Virus is approximately 80-120 nm in diameter. Virus is an envelope, single-stranded, with a segmented, negative sense RNA genome.

The three segments of the genome, the small (S), medium (M), and large (L) segments encode four different viral proteins i.e. the viral nucleocapsid (N) protein, two glycoprotein (G1 and G2), and the viral RNA ribonucleoprotein (RNP) respectively. The small segment encodes the viral nucleoprotein (N), Medium (M) segment encodes two envelop glycoprotein G1 and G2, which are responsible for neutralization and haemagglutination and the large segment encodes viral RNA dependent RNA polymerase which is associated with each RNP [17].

Species Affected

Domestic animals: Among domesticated animals, all breeds of sheep and goats are affected with this virus, whereas other livestock like cattle and buffaloes are resistant to infection. Ganjam virus, are highly pathogenic to exotic and crossbred animals and primarily infects goats [11].

Wild animals: A few fatal cases of the disease have been reported among blue duikers (*Cephalophus monticola*) in zoos or in the wild animals [4].

Transmission

GANV is tick-borne and mostly transmitted through the bite of any stage of the infected tick. Ganjam virus is primarily transmitted through the tick *Haemaphysalis intermedia*, *H. wellingtoni*, *R. haemaphysaloides*, and the mosquito *Culex vishnui* have also been described as competent vectors. Large numbers of other hard ticks (Ixodid ticks) are involved in the maintenance of the virus in nature and the virus can persist in the ticks for longer period, more than two years after they are infected. Transovarial transmission is reported by passing of the virus to offspring. All tick hosts are able to maintain the virus from one life stage to another life stage (transstadial transmission) [20].

Though, viruses are present in urine and feces of infected animals, direct contact do not result in infection [21].

Epidemiological Distribution

Global scenario: The virus and viral antibody, has been subsequently found in East Africa and it is now being most frequently reported from Kenya country between Nairobi and Mount Kenya as well as in Uganda, Tanzania, Somalia, Botswana, Mozambique and Ethiopia [22]. Now it is distributed in much wider geographical area in East Africa. Ganjam virus has now been reported from South Asian countries including India, Pakistan, and Sri Lanka. In 2013, disease was also reported in north-eastern China [5].

Indian scenario

Virus was first reported recovered from *Haemaphysalis intermedia* ticks collected from goats, suffering from lumbar paralysis during 1954-55 from Orissa and named after the place of isolation [3]. Now it has been prevalent in many states of India like Karnataka, Tamil Nadu, Andhra Pradesh, Punjab, Gujarat, Maharashtra, and Arunachal Pradesh and the virus was isolated from sheep, goats, cattle, ticks, mosquitoes and human [9].

Immunity

Virus can remain hidden in enzootic areas for years, in ongoing tick-host-tick cycles and be maintained by transovarial transmission with no manifestation of any disease problem. When sheep and goats are bred in areas where vector is prevalent remain often immune to disease. Maternal

antibodies protect their offspring from this disease [2]. When young animals are bitten by the infected ticks and exposed to the virus, they are protected by maternal antibodies and then gain their own protective antibodies. Disease is signaled whenever susceptible breeds of sheep and goats are introduced into the enzootic areas to improve the production potential of the indigenous breeds [6].

Morbidity and Mortality

Outbreaks are usually seen when animals with less immunity are exposed to the virus and can also be seen when ticks population temporarily expand their range during a period of heavy rainfall or other ecological change. The mortality rate ranges from 30–95 %. Very few animals who acquire infection recover once clinical signs are apparent. Ganjam virus affects breeds exotic to India and crossbred animals more severely, causing higher rates of mortality (75 % or higher) than indigenous populations. However, in general, Ganjam virus infections are milder than NSDV infections [20].

Pathogenesis

When vector takes a blood meal through bite from infected host, virus enters and replicate in gut of the arthropod vector. Subsequently, infection gets established and within few days or weeks virus appears in the saliva. The arthropod then remains infective throughout their life. The individual adult ticks could retain GANV infection for at least 871 days, and that larvae remain infective for 144 and nymphs at least 138 days [18]. After biting by the infected ticks, the infective saliva enters in the small capillaries or lymphatic of the vertebrate host like sheep, goats or human [14].

The virus having the particular predilection to the vascular endothelium cells of liver, spleen, lung, and other organs. Virus gets attached to the host receptor G1-G2, glycoprotein dimer, and then virus enters by clathrin-mediated endocytosis in to the host cell, followed by viral Ribonucleoprotein (RNPs) release from endosome. The virus replicates in the cytoplasm and synthesize viral RNA and proteins. They assemble to form new viral particle at Golgi membrane and are transported through secretory pathway to exit site at plasma membrane of host cell by process of budding. During the replication process, virus may cause cytopathic effect like endothelial swelling, congestion, edema and necrosis [15].

Clinical Findings

Clinical signs begin with a steep rise in body temperature (105-106°F) that persists for 1-3 days follows an incubation period of 4-5 days. Sometimes, the fever is biphasic. Leucopenia and viraemia usually coincide with the febrile phase of the disease, rapid breath, anorexia, depression followed by diarrhea. At onset of the disease there is profuse and watery diarrhea, later, bright to dark green feces mixed with blood and mucus may appear. Death may occur in the early febrile viraemic phase or follow two days after remission of the fever without showing any clinical sign. If animal survives, illness is manifested by dullness, depression, anorexia, ocular discharge. Conjunctivitis, mucopurulent blood stained nasal discharge and dyspnea. Death frequently occurs early in the course of the disease and is typically the result of hemorrhagic diarrhea and dehydration. Goats show similar clinical signs although with low severity when compared with the sheep [4].

Gross Pathology

On external examination of the carcass, presence of attached ticks on the body surface especially in the ear and head is the most striking feature. Conjunctivitis and dried crusts are usually present around the nostrils. Hindquarters are soiled with feces or a mixture of blood and feces. Dehydration is observed especially in animals with prolonged scouring. Petechial hemorrhages are observed in the coronary band above the hoofs^[1]. Petechial hemorrhages are observed on the nasal mucosa and there is excessive froth in the trachea. Relevant gross lesions further comprise congested and edematous lung, hydropericardium, hemorrhages on the serosal surfaces of epicardium and pale flaccid heart with unclotted blood^[15].

The pre-scapular lymph nodes on one side are notably enlarged and oedematous with subcapsular hemorrhages. Hemorrhagic diathesis is observed consisting of generalized petechial to ecchymotic hemorrhages present on serous surface and mucosal surface of various visceral organs. Catarrhal mucoid enteritis and hemorrhage with extensive ulceration is observed in the folds of the abomasum. Hemorrhagic gastroenteritis accompanied by petechial to ecchymotic hemorrhages on the mucosal surface of duodenum, ileocaecal valve, caecum and anterior part of colon have also been reported. In some cases earlier workers have reported hemorrhages seen as longitudinal striation or zebra striping in the lower gastric tract. Subserosal hemorrhage may be seen in the distended gallbladder, which contains thick syrupy bile. Extensive petechial to ecchymotic hemorrhages present on the sub capsular surface of mesenteric lymph nodes which are enlarged, hyperemic, and edematous^[15]. In long standing cases bone marrow of long bones becomes gelatinous and bright red. In pregnant ewes, the genital tract may be very hyperemic, fetal membranes may be swollen, edematous and hemorrhagic^[1].

Microscopic Pathology

The microscopic lesions in most of the tissues and organs are associated with the hemorrhage, together with some inflammatory changes and cellular infiltration. Hemorrhages and edema observed in the sub mucosa and muscular layer of gastrointestinal tract. Ulceration may be seen in the mucosa of ileum, caecum and colon. Petechial hemorrhages, distended capillaries packed with erythrocytes and increased thickness of the wall of ileocaecal junction. Streaks of congestion appear along with the folds of mucosa in the rectum. Hemorrhage, edema and generalized hyperplasia of superficial lymph node are prominent lesions. Germinal center hyperplasia along with some sub capsular hemorrhage of spleen follicle is noticed^[10].

Glomerular-tubular nephritis in the kidney is a constant feature. Degenerative changes occur in the glomeruli and convoluted and other tubules. Casts of desquamated cells appear in the lumen with much granular hyaline material. In the medullary area of the kidney, there is much congestion and swelling but the tubules themselves are not as severely affected as elsewhere^[1]. Petechial hemorrhages, edema and infiltration of inflammatory cells on the nasal and tracheal mucosa, congestion of lungs, subendocardial hemorrhage and myocardial degeneration were noticed^[15].

Diagnosis

The occurrence of a disease in sheep or goats with high mortality accompanied by a tick infestation is suggestive for GANV infection, especially if it follows movements into endemic areas or changes in tick populations^[4].

Clinical Diagnosis

Clinical diagnosis is on the basis of clinical signs and pathology, like nasal discharge in the sheep or goats and severe gastroenteritis. However, these clinical signs are common to other viral infection. A high incidence of illness in sheep with a low prevalence in goats is a characteristic feature of GANV infection but is not considered to be pathognomonic^[7].

Confirmative Diagnosis

Confirmation of suggestive signs and lesions requires detection of virus or antigen and antibodies in the clinical material is required to confirm the cause of disease by: -

Virus isolation: Ganjam virus can be isolated from material collected from infected animals by use of cell culture and this method is gold standard in virus diagnostics^[8]. For cell culture of virus, the BHK-21-C13 cell line is mostly used as culture medium. Vero cell line and primary and secondary lamb or hamster kidney cells are also been used for isolation. The strain of virus can be identified by production of cytopathic effect (CPE)^[11].

Agar gel immune diffusion test (AGID): It can be used as a valuable primary diagnostic tool for identification of virus antigen in the infected animal tissues like spleen, mesenteric lymph nodes etc. and brain of experimentally infected mice. Cross-reactions can occur with the antigens of other nairoviruses^[2].

Antibody detection: Various serological tests can be used to detect antibodies to virus. Paired serum samples should be collected to detect a rising titer. Indirect immunofluorescence is the most suitable assay for epidemiological studies and to study the response to experimental vaccines, but ELISAs can also be used. Complement fixation and indirect hemagglutination have also been employed, although rarely, Virus neutralization antibodies are often difficult to demonstrate. Cross-reactions can occur with other nairoviruses, especially Dugbe virus, in serological tests^[13].

Nucleic acid detection: The easiest and most sensitive method of confirmation of virus infection is reverse transcription polymerase chain reaction (RT-PCR) and it is quicker and does not require cell culture. The virus can be detected in the blood even after the animal's temperature has returned to normal. No commercial rapid tests to detect viral antigens are currently marketed^[21].

Differential Diagnosis

Clinical signs of this disease like hemorrhagic gastroenteritis, severe diarrhoea, nasal discharge, abortion and transient systemic problems are similar to other diseases or agent such as Peste des petits ruminants (PPR), Coccidiosis, Salmonellosis, Rift valley fever, cowdriosis and some toxicity like Arsenic poisoning in sheep and goats^[19].

Prevention and Control

Disease reporting and quick response is necessary for control the outbreaks in disease-free area. Veterinarians who suspect the infection should follow their national and local guidelines for disease reporting and state or federal veterinary authorities should be informed immediately. This virus can persist in an infected tick for more than two years; therefore, eradication is generally not feasible once the virus gets established in vector

populations and in areas where this disease is not endemic. The disease might be prevented by movement controls and quarantine of infected animals, together with tick control measures. Sheep and goats can be protected from tick vectors by dipping or spraying methods with an acaricide (eg. pyrethroids in grease, cypermethrin “pour-on” products, and various dip preparations) in the flock [4].

Vaccine

Modified-live virus vaccine attenuated in mouse brain, inactivated vaccine and experimental vaccine production, are under trial [2].

Treatment

Till now there is no specific treatment for this virus infection; however, supportive treatment, good shelter and quality feed may improve survival.

Public Health Significance

In India, the disease associated with GANV in human has never been reported at an epidemic level. However, a case of natural infection in a 12 year old European boy in Vellore, Tamil Nadu, and a few laboratory acquired cases have been reported. Antibodies to virus have also been found among the general population, laboratory workers and/or agricultural workers in Uganda, India and Sri Lanka. These virus infections might be acquired via tick bites, include needle or other means. It causes mild illnesses which resembles influenza like symptoms i.e. fever, shivering, headache, backache and abdominal pain, muscle pains, joint pains, nausea and vomiting. These, symptoms usually disappear after three days. Investigators should take precautions to prevent infections when working with these viruses [18].

Conclusion

Ganjam virus is a highly pathogenic, tick-borne, viral infection of sheep and goats characterized by hemorrhagic gastroenteritis and high mortality (90%) in susceptible population. It is transmitted by hard ticks, both transstadial and transovarian. It was originally thought to be endemic only in East Africa; particularly endemic in Kenya; but now it is reported from Asian subcontinents including India. It is assumed that the disease is vector transmitted, hence favorable environmental condition such as climate change, increase vector population coupled with decrease immune status of animals may spread the virus beyond their usual range and outbreak occurs where the disease has never been experienced before. If disease once occurs it may deteriorate the animal health and economy of farmers.

Rapid diagnostic test is currently limited to RT-PCR. No effective treatment and no any commercial vaccine are available for Ganjam virus disease. Hence, it can be controlled by only dipping or spraying of the animal by acaricides and controlling the potential vector by adopting the sanitary prophylaxis may help in combating this infection.

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