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Derleme

Akabane Virus Infection In Ruminants

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A B S T R A C T

Backround/Aim: This review includes that about Akabane virus infection which is a teratogenic agent to the ruminant fetuses. The virus is transmitted by *Culicoides* biting mosquitos, therefore is called arthropod-borne (Arbo) viruses. This infection is widely distributed in the countries where tropical climate zone prevails and causes in susceptible pregnant cattle, sheep and goats mainly abortion, stillbirth, and congenital abnormalities.

Conclusion: Akabane is an important disease that should not be forgotten due to their direct effects on animal health, reproductive efficiency and economic losses in the livestock industry.

Key Words: Akabane virus, ruminants, review.

Ruminantlarda Akabane Virus Enfeksiyonu

Ö Z E T

Özbilgi/Amaç: Bu derleme, ruminant fötuslarının teratojenik bir ajanı olan Akabane virusu enfeksiyonu hakkındadır. Virus, *Culicoides* cinsi sokucu sivrisineklerin ısırması yoluyla bulaşır, bu nedenle arthropod kaynaklı (Arbo) viruslar olarak adlandırılır. Bu enfeksiyon, tropikal iklim kuşağının hakim olduğu ülkelerde yaygın olarak görülmektedir ve duyarlı gebe sığırlarda, koyunlarda ve keçilerde genellikle abortus, ölü doğum ve doğuştan anormalilere neden olmaktadır.

Sonuç: Akabane, hayvan sağlığı, fertilite üzerine olan direkt etkileri ve hayvancılık endüstrisindeki ekonomik kayıplar nedeniyle unutulmaması gereken önemli bir hastalıktır.

Anahtar Kelimeler: Akabane virus, ruminantlar, derleme.

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History and Epidemiology of Akabane Virus Infection

The virus was first described and isolated from mosquitoes (JaGAr 39, prototype strain of Akabane virus obtained from *Aedes vexans* and *Culex tritaeniorhynchus*) in the summer of 1959 in Japan (Oya et al., 1961). For this reason, the virus was considered among arthropod-borne viruses. These infected midges during an outbreak in cattle were sampled from five areas in Gumma Prefecture, including the place of Akabane. However, no any association was made between this agent and this infection. In other outbreaks between 1972-1975 in Japan resulted in more than 42,000 cases of abortion, stillbirths and congenital malformations (arthrogryposis-hydranencephalie A-H syndrome) in cattle (Kurogi et al., 1975; Kurogi et al., 1976; Kono et al., 2008), thus it was established an etiological link for Akabane virus (AKAV) infection in ruminants (Wang et al., 2017). Congenital abnormality cases in calves have been described previously in some countries, for instance in Australia in 1957 (Whittem, 1957). Clinical and pathological features have resembled AKAV but, it could not be named, since the infection determined as AKAV. It has been reported AKAV infection from biting midges and affected animals around the world, for instance Australia (St George et al., 1978), Chinese Taipei (Liao et al., 1996), South Korea (Bak et al., 1980), Israel (Stram et al., 2004) and Turkey (Oğuzoğlu et al., 2015). It can be said AKAV widely distributed across the world in the Middle East, Asia, Australia, Africa and Japan, but not yet in the Americas.

Etiological features of AKAV

AKAV is an agent of Simbu serogroup belongs to the genus *Orthobunyavirus, Peribunyaviridae* family (Elliott and Blakqori, 2011; Plyusnin et al., 2012). The virus is transmitted by *Culicoides* sp. midges/mosquitoes just as like other members of Simbu serogroup (Ainovirus, Schmallenberg virus, etc.). The viral agent is enveloped, negative sense and tripartite single-stranded RNA genome, designated the large (L), medium (M), and small (S) RNA segments encodes the viral RNA dependent RNA polymerase, virion glycoproteins, and the nucleoprotein, respectively (Plyusnin & Elliott, 2011). The resistance of the AKAV to environmental conditions is very poor. It is reported that from USDA, the virus is destroyed by common disinfectants, such as hypochlorite (bleach), detergents, chlorhexidine, alcohol, and phenols, and are sensitive to temperatures above 50°C for 30 minutes.

The AKAV isolates have been classified into four genogroups (Kobayashi et al., 2007). Additionally, atypical AKAVs have been described (Yanase et al., 2018). In recent epizootics have been declared that it appears to be associated clinical signs with the changes of specific genogroup/lineage. Genogroup I was identified from calves showing neurological symptoms and which have the central nervous system disorders. Genogroup II was observed from adult bovine postnatal encephalomyelitis cases. All genogroups of AKAVs have neurovirulence feature and genogroup I strains neurovirulence greater than that of strains in genogroup II (Kono et al., 2008). For this reason, a hypothesis about the relationship between pathogenicity and genogroups, have been reported by some workers. Kono et al. (2008) were argued genogroup I strains might be involved not only in encephalomyelitis by postnatal infection but also in conventional teratogenicity by transplacental infection. Genogroups obtained from countries and isolation sources of some AKAV strains are summarized in table 1.

Changes in the manifestations of AKAV appear to be associated with a specific genogroup/lineage in recent epizootics.

Epizootiology

Simbu serogroup viruses replicate in both arthropod vectors and vertebrate hosts. AKAV is transmitted by hematophagous arthropod vectors they belong to the genus *Culicoides* of the family *Ceratopogonidae*. These vectors play an important role in transmitting AKAV and have a biological vector status, which are infected trans-ovarian and transmitted to their new generations. Some vectors have been specifically reported in the countries, for example, *Culicoides oxystoma* is considered the main vector in Japan (Kurogi et al., 1987). *C. brevitarsis* in Australia, and *C. milnei* and *C. imicola* in Africa have been reported (Doherty et al., 1972; Al-Busaidy et al., 1987).

AKAV can affect ruminant species, cattle, sheep, and goat. Additionally, antibodies to AKAV have been described in horses, donkeys, camels, deer, wild boar, antelope. The host range of AKAV infection is wide anymore, pigs and buffaloes have been found serologically positive (Al-Busaidy et al., 1987; Davies and Jessett, 1985). Viremia is very shortly in infected animals, duration changes from 1 to 6 days after infection.

Epizootics tend to occur at 4-6-year intervals in some areas, especially when immunity to previous infections of AKAVs has waned. The authors who are working with arboviruses predicted risk factors for the spread of these viruses. These are summarized in three main headings:

- Global warming,

- Global transportation and animal movement

- Human economic activities.

Clinical Signs and Pathogenicity

AKAV causes congenital abnormalities of the central nervous systems in newborn ruminants. Especially, AKAV is teratogenic to the fetus of ruminant species. If pregnant animals have not previously had exposure to the virus, has no specific immunologic reaction and therefore cannot protect. Transplacental infection occurs depending upon the stage of gestation and different congenital defects (infection at approximately 80-150 days of gestation in cattle and after 60 days of gestation in sheep and goat) may be observed in the fetus. These animals

Table 1. Some important AKAV strains and their sources.

Tablo 1. Bazı önemli AKAV suşları.

Strain name and Country	AKAV-Genogroup	Isolation source	Reference
JaGAr 39, Japan, 1959	II	*Aedes vexans*	Oya et al., 1961
OS 1/PI/08, Japan, 2008	II	Bovine placenta	Yanase et al., 2018
HS 1/Br/11, Japan, 2011	I	Porcine brain	Yanase et al., 2018
OBE 1, Japan, 1974	II	Bovine fetus	Kurogi et al., 1976; Kobayashi et al., 2007
R7949, Australia, 1978	III	*Culicoides brevitarsis*	Kobayashi et al., 2007
B8935, Australia, 1972	III	*Culicoides brevitarsis*	Doherty et al., 1972
MP496-KENYA, 1972	IV	*Anopheles funestus*	Kobayashi et al., 2007

can show that hydranencephalie (loss of cerebral hemispheres and the sacks filled with cerebrospinal fluid) and arthrogrypotyphosa or arthrogryposa (multiple articulation contractures/ deformity and rigidity of joints) (Whittem, 1957). The adult animals generally show not any specific clinical sign. Despite that, a few AKAV variants (like Iriki strain) can affect adult cattle and can cause neurological signs (named epizootic encephalomyelitis) due to postnatal infection (Miyazato et al., 1989; Hayama et al., 2016).

The clinical effects of neurotrophic arboviruses such as AKAV vary from seasonal formation over a large area to histopathological findings of affected animals. Clinical signs have been noted as astasia, ataxia, opisthotonus, kyphosis, scoliosis, and hypersensitivity in transplacental affected animals.

Immunity

In natural infection in adult animals after shortly viremia period produce the neutralizing antibodies, which are detected by serologically 14 days after infection. While a single dose live attenuated vaccine induces an effective immunity, inactivated vaccines require two-step vaccination.

Diagnosis

AKAV infection listed in Office International des Epizooties (OIE) (Chapter 2.9.1- Bunyaviral diseases of animals) and in Terrestrial Manual 2014 have been declared that diagnosis is possible usually from the blood of viraemic animals, from vector pools and occasionally from aborted fetal materials. It is rarely made the virus isolation for diagnosis of infection. In this field, the nucleic acid-based diagnosis has predominantly advanced. Serological diagnosis by using virus neutralization and immunofluorescence techniques have included in some laboratories for AKAV infection (Blacksell et al., 1997; Gard et al., 1988). Virus isolation in cell culture has been done by using Vero, BHK-21, and *Culicoides* cell lines. For AKAV nucleic acids detection have been developed a nested RT-PCR technique from Akashi et al. (1999).

Control and Prevention

AKAV infection is the causative agents of significant morbidity and mortality among ruminants globally. The agent is an arbovirus and maintained in complex biological life cycles, involving a primary vertebrate host and a primary arthropod vector. AKAVs are unique, in that they must be able to infect and replicate in both invertebrate (*Culicoides sp*.) as well as vertebrate hosts in order to maintain a successful viral lifecycle. Therefore the basis of the control and prevention programs around the World about AKAV infection is based primarily on the vector struggle. Biocontrol is an ecologically friendly method and can be an attractive alternative to more conventional vector control strategies that involve insecticides due to its potential to have minimal impact on the environment. Huang et al. (2017) have been reported that three predators generally used in biological control of mosquitoes. Fish (*Gambusia affinis*), larvae of *Toxorhynchites* species mosquitoes and Copepods (mainly *Mesocyclops* and *Macrocyclops* species) have been used as predators to inhibit arboviral replication in mosquitoes.

RNA interference (RNAi) based strategies play a central role as a new alternative method for controlling arbovirus infections in arthropod vectors (Donald et al., 2012; Kean et al., 2015). In this context, exogenous small RNAs can be used to stimulate antiviral effectors invertebrate hosts.

Vaccination is the most effective measure to minimize livestock loss. Commercial vaccines against Akabane, Aino, Chuzan, Ibaraki and bovine ephemeral fever viruses are available in Japan. Both live attenuated and inactivated vaccines have been used against AKAV infection for prevention.

AKAV infection in Turkey

The end of 1979 has been firstly reported AKAV infection in affected calves from Aydın province characterized by arthrogryposis, hydranencephaly, and torticollis (Urman et al, 1980; Taylor and Mellor, 1994). After a long time, perhaps due to climate change and global warming, in recent years the presence of AKAV infection in ruminants in Turkey has been frequently and increasingly reported (Oguzoglu et al., 2015; Şevik, 2017a,b). The virus strains were molecularly characterized and genogroup 1 and 2 AKAVs were identified in mentioned studies.

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Akabane Standard Operatıng Procedures: 1. Overvıew Of Etıology And Ecology. https://www.aphis.usda.gov/animal_health/emergency_management/downloads/sop/sop_akabane_ee.pdf