BOVINE VIRAL DIARRHEA AND MUCOSAL DISEASE COMPLEX

Bovine viral diarrhea (BVD) is most common in young cattle (6–24 mo old).

The clinical presentation can range from inapparent or subclinical infection to acute and severe enteric disease to the highly fatal mucosal disease complex characterized by profuse enteritis in association with typical mucosal lesions.

BVD must be distinguished from other viral diseases that produce diarrhea and mucosal lesions. These include malignant catarrhal fever (see Malignant Catarrhal Fever), which usually is a sporadic disease in more mature cattle, bluetongue (see Bluetongue), and rinderpest (see Rinderpest), which is currently considered to be eradicated worldwide.

Bovine viral diarrhea virus (BVDV), the causal agent of BVD and mucosal disease complex, is classified in the genus *Pestivirus* in the family Flaviviridae.

Although cattle are the primary host for BVDV, several reports suggest most even-toed ungulates are also susceptible.

Classically, isolates of BVDV are separated into noncytopathic and cytopathic biotypes based on their ability or lack of ability to cause overt cytopathic change and cell death in cell cultures.

Noncytopathic BVDV is the predominant viral biotype in nature, whereas cytopathic BVDV is relatively rare and of little epidemiologic relevance.

The cytopathic biotype arises in cattle that are persistently infected with noncytopathic biotype of the same or a genetically similar BVDV strain. The switch in biotype is the result of mutations that often involve recombination of noncytopathic viral RNA with itself, with heterologous viral RNA, or with host cell RNA.

ETİOLOGY AND EPİDEMİOLOGY:

Serologic surveys conducted throughout the world suggest that BVDV is endemic in the cattle population of most cattle-producing countries. In some countries, BVD is considered the single most important viral infection of cattle.

The prevalence of antiviral antibody in cattle varies greatly among countries and geographic regions because of differing cattle housing practices, population densities, vaccination practices, and implementation of different control or eradication programs. Prevalence of antiviral antibody may be >90% if vaccination is practiced commonly in a geographic region. Although cattle of all ages are susceptible, most cases of overt clinical disease are seen in cattle between 6 mo and 2 yr old.

CLİNİCAL FİNDİNGS AND LESİONS:

Disease induced by BVDV varies in severity, duration, and organ systems involved. Infection of immunocompetent susceptible animals with either noncytopathic or cytopathic BVDV is termed acute or transient BVD.

Inapparent or subclinical infection without any clinical signs that is followed by seroconversion is the most common form of infection in the field. Acute clinical disease may range from mild disease of high morbidity and low mortality to severe enteric disease with considerable mortality.

Biphasic fever (~104°F [40°C]), depression, decreased milk production, transient inappetence, rapid respiration, excessive nasal secretion, excessive lacrimation, and diarrhea are typical signs of acute clinical BVD.

Clinical signs of disease usually are seen 6–12 days after infection and last 1–3 days. Transient leukopenia may be seen with onset of signs of disease. Recovery is rapid and coincides with production of viral neutralizing antibody.

Gross lesions seldom are seen in cases of mild disease. Lymphoid tissue is a primary target for replication of BVDV, which may lead to immunosuppression and enhanced severity of intercurrent infections.

Some isolates of BVDV (BVD type 2) have been associated with severe clinical disease that manifests as high fever (~107°F [41°–42°C]), oral ulcerations, eruptive lesions of the coronary band and interdigital cleft, diarrhea, dehydration, leukopenia, and thrombocytopenia.

In thrombocytopenic cattle, petechial hemorrhages may be seen in the conjunctiva, sclera, nictitating membrane of the eyes, and on mucosal surfaces of the mouth and vulva.

Prolonged bleeding from injection sites also occurs. Swollen lymph nodes, erosions and ulcerations of the GI tract, petechial and ecchymotic hemorrhages on the serosal surfaces of the viscera, and extensive lymphoid depletion are associated with severe forms of acute BVD.

The duration of overt disease may be 3–7 days. High morbidity with a mortality of ≥25% is common. Severity of acute BVD is related to the virulence of the viral strain infecting the animal and does not depend on viral biotype.

Persistent infection is an important sequela of fetal infection with noncytopathic BVDV. Persistently infected calves may appear healthy and normal in size, or they may show stunted growth and be prone to respiratory or enteric ailments. They often have a short life span, and death before 2 yr of age is common.

Persistently infected cows always give birth to persistently infected calves, but most calves sired by a persistently infected bull will not be infected with virus in utero.

Lesions attributable to BVDV often are not seen in persistently infected cattle at necropsy. Antibody against BVD seldom is detected in persistently infected cattle in the absence of vaccination or superinfection with an antigenically heterologous BVDV.

Persistently infected cattle exposed to BVDV that is antigenically different from their resident noncytopathic virus can produce antiviral antibody. Therefore, screening for persistent infection using serologic tests to identify animals that lack antiviral antibody may not detect some persistently infected cattle.

Mucosal disease is an uncommon but highly fatal form of BVD occurring in persistently infected cattle and can have an acute or chronic presentation. Mucosal disease is induced when persistently infected cattle become superinfected with cytopathic BVDV.

The origin of the cytopathic BVDV is usually internal, resulting from a mutation of the resident persistent, noncytopathic BVDV. In those cases, the cytopathic virus is antigenically similar to the resident noncytopathic virus. External origins for cytopathic BVDV include other cattle and modified-live virus vaccines.

Cattle that develop mucosal disease due to exposure to a cytopathic virus of external origin often produce antiviral antibody. Prevalence of persistent infection usually is low, and many persistently infected cattle do not develop mucosal disease, regardless of exposure.

Acute mucosal disease is characterized by fever, leukopenia, dysenteric diarrhea, inappetence, dehydration, erosive lesions of the nares and mouth, and death within a few days of onset.

At necropsy, erosions and ulcerations may be found throughout the GI tract. The mucosa over Peyer's patches may be hemorrhagic and necrotic. Extensive necrosis of lymphoid tissues, especially gut-associated lymphoid tissue, is seen on microscopic examination.

DİAGNOSİS:

BVD is diagnosed tentatively from disease history, clinical signs, and gross and microscopic lesions. Diagnostic laboratory support is required when clinical signs and gross lesions are minimal. Laboratory support also is required in some outbreaks of mucosal disease or clinically severe acute BVD, because either disease may appear similar to rinderpest (see Rinderpest) or malignant catarrhal fever (see Malignant Catarrhal Fever).

Laboratory tests for BVDV include isolation of virus or viral antigen in clinical specimens and tissues, and assays that detect anti-BVDV antibody in serum or milk. Because antibody against BVDV can be highly prevalent in regions with high infection prevalence and/or common use of BVD vaccines, a single serologic test is seldom sufficient for diagnosis of recent infection. A >4-fold increase in antibody titer in paired serum samples obtained ≥2 wk apart is necessary to verify recent infection.

Isolation of BVDV from blood, nasal swab specimens, or tissues confirms active infection. Identification of persistent infection requires detection of virus in clinical specimens obtained at least 3 wk apart. Colostral antibody can impair the sensitivity of virus isolation in blood during the first weeks of life. At necropsy, tissues of choice for viral isolation include spleen, lymph node, and ulcerated segments of the GI tract.

Alternatives to viral isolation include antigen-capture ELISA to detect virus in blood, serum, or tissue biopsies; immunohistochemistry to detect viral protein in frozen or fixed tissues; PCR to detect viral RNA in clinical specimens; and PCR or in situ hybridization to detect viral RNA in fresh or fixed tissues.

Differentiation of viral genotypes and subgenotypes may be accomplished by PCR assays alone, or by PCR assays followed by analysis of nucleotide sequence, restriction fragment analysis, or palindromic nucleotide substitution analysis.

Monoclonal antibody binding assays and viral neutralization assays also differentiate viral genotypes.

TREATMENT AND CONTROL:

Treatment of BVD remains limited primarily to supportive therapy. Control is based on sound management practices that include use of biosecurity measures, elimination of persistently infected cattle, and vaccination.

Replacement cattle should be tested for persistent infection before entry into the herd.

Quarantine or physical separation of replacement cattle from the resident herd for 2–4 wk should be considered, and vaccination of replacement cattle for BVD should be done before commingling with the resident herd.

Embryo donors and recipients also should be tested for persistent infection. If vaccination of embryo donors or recipients is warranted, it should be done at least one estrous cycle before embryo transfer is performed.

Because BVDV is shed into semen, breeding bulls should be tested for persistent infection before use. Artificial insemination should be done only with semen obtained from bulls free of persistent infection.

Screening cattle herds for persistent infection can be done by PCR assays using skin biopsies, blood, or milk; by classical virus isolation methods using serum or buffy coat cells; by antigen-capture ELISA using serum, buffy coat, milk, or skin biopsies; or by antigen detection using immunochemical methods on tissue or skin biopsies.

Several strategies, based on herd size, type of herd being screened, financial limitations of the herd owner, and testing ability of the diagnostic laboratory being used, are available to screen herds for persistent infection.

When identified, persistently infected cattle should be removed from the herd as soon as possible, and direct or indirect contact with pregnant cattle should be prevented.

Inactivated and modified-live virus vaccines are available. They contain a variety of strains of BVDV representing both viral biotypes and viral genotypes 1 and 2. Antigenic diversity among BVDV may affect the efficacy of a given vaccine if the vaccine virus or viruses differ significantly from the challenge virus.

Proper and safe immunization of cattle with either inactivated or modified-live virus vaccines requires adherence to the manufacturer's instructions. Because BVDV is fetotropic and immunosuppressive, use of modified-live virus vaccines is not recommended in cattle that are pregnant or showing signs of disease.

Inactivated viral vaccines may be used in pregnant cattle. Protection conferred by inactivated vaccines may be of short duration, and frequent vaccination may be necessary to prevent disease or reproductive failure.

Colostral antibody confers partial to complete protection against disease in most calves for 3–6 mo after birth. Vaccination of neonatal cattle that have acquired colostral antibody may not stimulate a protective immune response, and revaccination at 5–9 mo of age may be necessary.

A booster dose of vaccine is often administered before first breeding, and additional booster doses of vaccine may be administered in subsequent years before breeding.