Pathogenicity of Cytopathic Strains (NADL, Camel) of Bovine Viral Diarrhoea Virus (BVDV) in Experimentally Infected Pregnant Goats

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ABSTRACT

The aim of this study was to investigate the pathogenicity of bovine viral diarrhea virus (BVDV) on the internal organs of pregnant goats. Thirteen healthy pregnant goats free from BVD neutralizing antibodies were used in this study. Animals of the first and second groups were inoculated I/V and I/P with two cytopathic strains of BVD virus, NADL and camel respectively at about 65 days of gestation. The third group was kept as control. Blood samples were collected and the serum was separated for serum neutralization test. Tissue specimens from liver, kidneys, lungs, heart, spleen, small & large intestine, abomasum, and supramammary & mesenteric lymph nodes of pregnant does were taken for histopathological examination. Clinically, all infected goats developed mild serous nasal discharges, pyrexia and diarrhea. In NADL strain of BVDV group, abortion occurred in 3 out of 5 does at 7, 17 and 21 days post inoculation (PI) of virus. In camel strain of BVDV group, 1 out of 4 does aborted one fetus at 65 days PI. The histopathological examination of liver showed multiple foci of hepatic cell necrosis associated with aggregations of mononuclear cells. Kidneys of does inoculated with NADL strain showed hypercellularity of glomerular tuft with adhesion to the Bowman's capsule in addition to focal thickening of glomerular capillary basement membrane (membranoproliferative glomerulonephritis). Foci of chronic interstitial nephritis were also seen in camel strain of BVDV group. In lungs, multiple areas of alveolar emphysema accompanied with areas of chronic interstitial pneumonitis were seen. The intestinal lesions of both infected groups were primarily inflammatory in nature and characterized by desquamation of epithelium lining of mucosa, highly infiltration of oedematous lamina propria with mononuclear cells, in addition to mucous degenerative changes of epithelium lining of intestinal crypts. The lymphoreticular tissues (spleen, lymph nodes and Peyer’s patches) showed severe lymphocytic cell depletion. Neutralizing antibodies against BVDV were detected in the sera of all infected animals of both groups. Immunofluorescent finding revealed presence of viral antigen in various tissues of all infected does. It could be concluded that BVD virus infection induced pronounced histopathological changes in visceral organs of pregnant goats, in addition to its adverse effect on the reproductive performance. Moreover, severe lymphoid depletion developed in lymphatic organs. Viral antigen was also detected within the various tissues by immunofluorescent technique.

Key words: BVDV, goats, histopathology, abortion, immunofluorescence, kidney, liver, heart, lung, spleen, ileum, lymph nodes.

Introduction

Bovine viral diarrhea virus (BVDV) is a single-stranded, round-shaped RNA virus, member of genus Pestivirus, which also includes classical swine fever virus and border disease virus, within the Flaviviridae family. The virus is divided into two genotypes (BVDV-1 and BVDV-2) on the basis of antigenic and genetic differences (Baker, 1995 and Fauquet et al., 2005). Two biotypes of BVDV were categorized as cytopathogenic or non-cytopathogenic based on their activity in cell culture (Baker, 1995). Strain heterogeneity and differences in pathogenicity may have a determinant role in the...
Infection with BVDV can result in severe economic and reproductive losses, especially in cattle industry (Lamm, et al. 2009). Moreover, BVDV causes immunosuppression and digestive and respiratory disorders in cattle (Grooms et al., 2002).

Goats have been reported to be infected with BVDV under natural and experimental conditions (Depner et al., 1991; Loken and Bjerkas, 1991; Wohlsein et al., 1992; Broadus et al., 2009; Lamm et al., 2009 and Desouky et al., 2009& 2011 and Passler et al., 2014). These studies indicated that pregnant goats are susceptible to cytopathic and non-cytopathic BVDV infection that resulted in reproductive dysfunction with abortions, fetal resorption, mummification, stillbirth and weak newly born kids with congenital defects and pathological changes. A study demonstrated that non pregnant goats seroconverted after natural exposure to BVD persistently infected cattle. (Broadus et al., 2007). On the other hand, there is no available literature and data concerning the histopathological effects of different serotypes of BVDV infection in different body organs of pregnant goats except for its fetopathogenic effect on the reproduction. However, the most pronounced histopathological changes of BVDV in experimentally infected calves were multifocal areas of consolidation in lungs with interstitial pneumonia (Galav et al., 2007 and Glotov et al., 2016), mild gastroenteritis with erosion and ulceration of mucosa, oedema and hemorrhages in the alimentary tract (Ellis et al., 1998), lymphoid depletion of lymph nodes, spleen and Peyer’s patches (Liebler-Tenorio et al., 2002& 2004; Galav et al., 2007; Raizman et al., 2011 and Wang et al., 2014), Kidney lesions were membranoproliferative glomerulonephritis (Cutlip et al., 1980 and Galav et al., 2007). Therefore, the main objective of this study was to investigate the pathogenicity of BVDV in the visceral organs of pregnant does inoculated with cytopathic strain of either bovine (NADL) or camel origin, in addition to detection of virus using the immunofluorescent technique.

**Materials and Methods**

**Animals:**

The present work was done on 13 healthy pregnant goats free from BVD virus neutralizing antibodies, brucella and parasitic infestation. Their ages ranged from 12-24 months old and body weight ranged from 18-20 kg.

**Virus inoculum:**

Two cytopathic strains of BVD virus were used.

a- National Animal Disease Laboratory (NADL) strain of BVD virus of bovine origin. The titre of this strain was $10^9$ tissue culture infective dose (TCID$_{50}$) per ml.

b- Camel strain of BVD virus. The titre of this strain was $10^{11}$ tissue culture infective dose (TCID$_{50}$) per ml. Both strains of BVD virus were propagated and titrated in Madin-Darby bovine kidney cell line (MDBK).

**Experimental design:**

The animals were divided into three groups:

**Group I** included 5 animals, each doe was inoculated with 10ml {5ml I/V and 5ml I/P} of tissue culture suspension of NADL strain containing $10^9$ TCID$_{50}$ per ml at about 65 days of gestation. **Group II** comprised 4 animals; each doe was inoculated with 10ml {5ml I/V and 5ml I/P} of tissue culture suspension of camel strain containing $10^{11}$ TCID$_{50}$ per ml at about 65 days of gestation. **Group III** consisted of 4 animals which were kept non infected along the whole period of experimental work and served as control. Following inoculation; pregnant does were kept under daily observation throughout experimental period for any clinical manifestations. Also, all animals were penned separately and kept at the same managemental conditions and under complete quarantine and preventive measures.
Collection of blood sample:

Blood samples were collected aseptically through jugular vein puncture at day after day during the first week post inoculation (PI), followed by weekly sampling from pregnant goats till kidding. Serum samples were harvested by centrifugation at 3000 rpm for 10 min. and kept frozen at -20 °C till used for serum neutralization test.

Serum neutralization test (SNT):

The test was done using Beta procedure (constant amount of virus– variable dilution of serum) according to Frey and Leiss (1971).

Histopathological Studies:

Specimens from liver, kidneys, lungs, heart, spleen, small & large intestine, abomasum, and supramammary and mesenteric lymph nodes were taken from the pregnant does following abortion and/or normal kidding and fixed in 10 % neutral formalin. Paraffin sections of 4 – 5 microns were prepared and stained with hematoxylin and eosin after Bancroft et al. (1996).

Fluorescent microscopical method:

The direct immunofluorescent antibody technique was adopted by Goldman (1968) as rapid confirmatory method to detect the BVDV within the tissues. Cryostat sections of freeze-dried tissues of spleen, mesenteric lymph node, ileum and kidneys of pregnant does were fixed in chilled acetone for 15 min. Using polyclonal bovine antiserum conjugated with fluorescein isothiocyanate (FITC) against BVDV. This serum was applied on sections of tissues and incubated at 37°C for 30-60 min in a humid chamber for reactivity with antigen. The sections were washed off gently in three changes of phosphate buffered saline with pH.7.2. After being air–dried, the stained sections were examined with fluorescence microscope and the sites of antigen–antibody reaction were expected as bright green fluorescence.

Results

Clinical signs:

In NADL strain of BVDV group, abortions occurred in 3 out of 5 does inoculated with the virus at 7, 17, and 21 days PI of virus at 65 days of gestation. In camel strain of BVDV group, 1 out of 4 does aborted one fetus at 65 days PI. Reproductive performance and the pathological effects of BVDV on genital organs (ovary, uterus and placenta) as well as the newly born kids were previously studied in details and published before (Desouky et al., 2009 &2011).

Except for reproductive failure, there was evidence of febrile response immediately following inoculation of the virus in both infected groups. In NADL strain group all does developed first phase of pyrexia on the 1st day PI. The second phase of pyrexia was observed at 5 and 7 days PI and return to the pre-inoculation value at 14 days PI. In camel strain group the first peak of temperature was noticed on the 1st day PI followed by second peak on the 5th day PI that continued up to 28 days PI and the third peak was at 42 and 49 days PI followed by declination in temperature till the end of gestation.

Moreover, profuse watery diarrhea was observed in 2 out of 5 does inoculated with NADL strain group. There were severe depression and variable anorexia. In the first case, diarrhea was developed as early as on the 5th day PI and followed by abortion on 7th day PI. The second doe revealed diarrhea on 8th
day PI and continued for about 4-5 days and followed by abortion. The third case of abortion showed no signs of diarrhea. The remaining 2 does that continued the gestation till kidding and does inoculated with camel strain of BVDV showed mild and intermittent diarrhea during the whole period of gestation. Mild serous nasal discharges were also noticed in all infected does.

Postmortem findings:

NADL strain of BVDV group:

There was congestion at corticomedullary junction of kidney of aborted goats. The liver was congested and enlarged in size. The different parts of the gastrointestinal tract were generally appeared within the normal limit. However, the mesenteric lymph nodes were oedematous and enlarged in size. Furthermore, the supramammary lymph nodes showed haemorrhages and oedema (Fig.1). In lungs, minor areas of consolidation accompanied with alveolar and interlobular emphysema were observed in one case.

Camel strain of BVDV group:

In all examined cases the supramammary, iliac, mesenteric, prescapular and lumbar lymph nodes showed variable degrees of oedema and haemorrhages. There were petechial haemorrhages at ileocecal junction. Congestion and hyperemia of abomasum and congestion at corticomedullary junction of kidney were observed. Lungs showed multifocal areas of consolidation. The gross appearance of small and large intestine, spleen, and heart was within the normal limit.

Serum neutralization test:

In NADL strain of BVD group, the neutralizing antibodies (NAbs) against virus were detected in sera of 2 out of 5 inoculated does as early as 3 days PI, while the remaining does were also seroconverted at 14 days PI. Two does showed the highest titre of Nabs (1/128) at 21 and 35 days PI.

In camel strain of BVD group, all does developed NAbs against virus in their sera at 21 days PI. The highest titre of NAbs (1/64) was recorded in 2 does at 35 and 56 days PI.

Histopathological findings:

Liver:

Histopathological examination of the liver of both inoculated groups revealed that hepatic cells were diffusely swollen, finally granulated and vacuolated with thickening of cell membrane giving the picture of ground glass like appearance. Multiple foci of hepatic cell necrosis associated with mononuclear cell infiltration and activation of Kupffer cells were seen (Fig.2). There were excessive aggregations of neutrophils in hepatic blood vessels, in addition to luminal accumulation and pavementation of endothelial cells lining the hepatic sinusoids with numerous number of neutrophils was also observed. Excessive round cell infiltration in portal areas associated with hyperplasia of the epithelium lining of bile duct was seen.

Kidneys:

In both inoculated groups, the renal glomeruli showed hypercellularity of glomerular tuft with obliteration of the capillary lumina and adhesion between the glomerular tufts to the parietal layer of Bowman’s capsule (Fig.3). Moreover, focal thickening of glomerular capillary basement membrane was
observed (membranoproliferative glomerulonephritis). In medulla, linear aggregations of neutrophils in intertubular spaces associated with peritubular congestion and haemorrhages were noticed. In most cases extensive medullary congestion and haemorrhages were clearly observed. Some of renal blood vessels showed thickening in their wall accompanied with hypertrophy of endothelial cells and narrowing or occlusion of lumen, besides to perivascular oedema and round cell aggregation were seen. In camel strain of BVDV group, renal glomeruli showed occasionally shrunken and atrophied glomerular tuft accompanied with dilatation of Bowman’s capsule (glomerulocystic change) and accumulation of serous exudates within the capsular space. In one case, there were foci of chronic interstitial nephritis (Fig.4). These foci were characterized by periglomerular and intertubular mononuclear cells infiltration in interstitial tissue associated with fibrous tissue proliferation. Renal tubules were atrophied, while others appeared cystically dilated. Proteinous casts were occasionally seen within the lumen of some tubules associated with necrobiotic changes of the epithelium lining of tubules.

Lungs:

In both inoculated groups, multiple areas of alveolar emphysema accompanied with areas of chronic interstitial pneumonitis were observed. Moreover, endarteritis obliterans of pulmonary blood vessels was seen. The B.V. appeared concentrically thickening in its wall associated with occlusion of lumen and perivascular aggregations of mononuclear cells (Fig.5). In some cases, intraluminal accumulation and pavement of endothelial cells lining of bronchial B.V. with leukocytes mainly neutrophils were also noticed.

Heart:

Microscopical examination of heart in both inoculated groups showed focal aggregations of mononuclear cells in between the cardiac muscle fibers (Fig.6). The blood vessel appeared dilated and congested.

Spleen:

In both inoculated groups. There was marked depletion of lymphoid tissue in the external zone of Malpighian corpuscles (Fig.7), in addition to the lymphocytes appeared smaller and pyknotic. The red pulp was extensively infiltrated with neutrophils aggregations particularly around the lymphoid follicles. In camel strain of BVDV group, there were multiple foci of haemosidrosis within the red pulp. Deposition of brown irregular shaped granules in phagocytic cells (siderocytes) associated with fibrous C.T. proliferation (siderofibrosis) were occasionally seen.

Supramammary and mesenteric lymph nodes:

In both inoculated groups, there was marked lymphocytic depletion in cortex and medulla. The germinal centers of almost all lymphoid follicles were entirely replaced by vacuolated histiocytic cells associated with deposition of fibrillated homogenous eosinophilic structureless material and individual cell necrosis (Fig. 8). The medullary and subcapsular sinuses were widely dilated and highly populated with foam cells of histiocytic origin. In camel strain of BVDV group, the medullary sinuses were also dilated and distended with lymph and round cell aggregations (lymph catarrh).
Fig. 1: Supramammary lymph node of pregnant doe inoculated with NADL strain of BVDV, showing oedema, and haemorrhages at the periphery of lymph node.

Fig. 2: Liver, showing focal area of hepatic cell necrosis associated with aggregations of mononuclear cells in hepatic parenchyma and activation of Kupffer cells. (H&E stain, X250).

Fig. 3: Kidney, showing hypercellularity of glomerular tuft and adhesion of glomerular tuft to Bowman's capsule (H&E stain, X250).

Fig. 4: Kidney, showing focal area of chronic interstitial nephritis (H&E stain, X100).

Fig. 5: Lung, showing endarteritis obliterans associated with perivascular aggregations of mononuclear cells. (H&E stain, X250).

Fig. 6: Heart, showing focal aggregations of mononuclear cells in between the cardiac muscle fibers. (H&E stain, X250).

Fig. 7: Spleen, showing depletion of lymphoid tissue in external zone of Malpighian corpuscles, in addition to, lymphocytes were small and pyknotic. (H&E stain, X250).

Fig. 8: Supramammary lymph node showing individual lymphocytic cell necrosis and vacuolated histiocytic cells in germinal center of lymphoid follicle. (H&E stain, X400).
Small intestine:

Jejunum:

Showed denudation of its epithelial cells lining of villi (Fig.9). Mononuclear and eosinophilic cells infiltration were seen at the tips of denuded villi and in lamina propria associated with oedema, petechial haemorrhage and congestion of blood capillaries at the villous core. No pronounced histopathological changes could be detected in jejunum in camel strain of BVDV group. The microscopical examination of duodenum in both inoculated groups appeared within the normal limit.

Ileum:

In both inoculated groups, microscopic examination showed partial desquamation of epithelium lining of mucosa especially at the tips of villi associated with round cell aggregations in lamina propria. The lymphoid follicles (Peyer’s patches) showed moderate lymphocytic depletion and /or extensive necrosis and lymphatic tissue was replaced by homogenous eosinophilic substance and infiltrated with macrophage and neutrophils (Fig.10).

Ileocecal junction:

In NADL strain of BVDV group, there was focal desquamation of epithelium lining of mucosa. The lamina propria was oedematous and moderate infiltrated with leukocytes mainly eosinophils. The epithelium lining of intestinal crypts showed mucous degenerative changes (Fig. 11). The lymphoid tissue was diffusely infiltrated with neutrophils and eosinophils associated with intraluminal aggregation of neutrophils within the intestinal glands which appeared necrosed .Numerous globule leukocytes within the lamina propria and epithelial cells lining of intestinal crypts were observed. In camel strain of BVDV group, the mucosa of ileocecal junction appeared intact. There were excessive aggregations of mononuclear cells at the tips of villi and lamina propria associated with increase in mucous producing cells (goblet cells) in the intestinal crypts (Fig.12).

Large intestine:

Cecum:

In NADL strain of BVDV group, the microscopic examination revealed focal desquamation of epithelium lining of the mucosa. The lamina propria was oedematous and highly cellular infiltrated with inflammatory cells mainly eosinophils, lymphocytes plasma cells and neutrophils. Some of the crypts of Lieberkuhn showed intraluminal aggregations of neutrophils and necrotic epithelial cells while others showed mucous degeneration of epithelium lining accompanied with interstitial edema and extensive periglandular mononuclear cells and numerous eosinophilic cell aggregations (Fig.13).

The microscopic examination of colon appeared within the normal limit. On the other hand, no pronounced histopathological changes could be detected in cecum and colon in camel strain of BVDV group.

Abomasum:

In one case of camel strain of BVDV group, there was focal desquamation of epithelium lining of mucosa .Lamina propria and submucosa were highly infiltrated with mononuclear cells, in addition to intensive congestion and slight oedema among the abomasal glands. Multiple necrotic foci in abomasal glands associated with leukocytic cell infiltration mainly neutrophils were clearly noticed.
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(Fig. 14). In NADL strain of BVDV group, the microscopical examination of abomasum appeared within the normal limit.

Fig. 9: Jejunum, showing denudation of epithelium lining of villi associated with aggregation of mononuclear and eosinophilic cells in lamina propria (H&E stain, X100).

Fig. 10: Ileum, Peyer’s patches, showing lymphocytic depletion and lymphatic tissue was replaced by homogenous eosinophilic substance (H&E stain, X400).

Fig. 11: Ileocecal junction, showing mucous degenerative changes of epithelium lining of intestinal crypts associated with oedema and moderate aggregations of leukocytes mainly eosinophils in lamina propria (H&E stain, X400).

Fig. 12: Ileocecal junction, showing an increase in mucous producing cells (goblet cells) in the intestinal crypts (H&E stain, X100).

Fig. 13: Cecum, showing mucous degeneration of epithelium lining of crypts associated with intraluminal aggregations of necrotic epithelial cells and neutrophils, in addition to interstitial oedema and periglandular mononuclear and eosinophilic cell aggregations (H&E stain, X400).

Fig. 14: Abomasum, showing focal necrotic area in abomasal glands accompanied with leukocytic cell infiltration mainly neutrophils (H&E stain X100).

Fig. 15: Spleen, showing few positive reacting macrophages in the red pulp. (Direct immunofluorescent (DIF) stain X400).

Fig. 16: Mesenteric lymph node showing numerous specific positive reacting cells in the interfollicular cortical area. (DIF stain X250).
Immunofluorescent findings:

The presence and distribution of BVD viral antigen in organs of experimentally infected does with either NADL or camel strain of BVDV were nearly the same in each organs but differed in the degree of intensity of fluorescence ranging from faint to moderate reaction. In spleen, the antigen was identified in small round cells (lymphocytes) in white pulp. Also, the antigen was detected in few scattered macrophages in the red pulp (Fig.15). Mesenteric lymph nodes showed faint to moderate fluorescent reacting cells in the germinal centers of lymphoid follicles. The antigen was also observed in scattered population of lymphocytes and reticular cells in the inter follicular cortical area and paracortical area (Fig.16). Moreover, a few moderate number of positive cells mainly comprising macrophages in medullary cords were seen. In ileum, there was faint intensity of specific positive reaction in the epithelial cell lining of villi and crypts and in the lymphocytes located in lamina propria. Moderate intensity of positive fluorescence in numerous cells within the Peyer’s patches was observed. In kidney, presence of faint intensity of fluorescent reaction in few lymphocytes scattered in the renal interstitial tissue was noticed. A specific reaction was found occasionally within glomerular tuft, in endothelial cells of blood vessels, in perivascular lymphocytes and in epithelial cells of renal tubules.

Discussion

The present work was carried out to clarify the pathogenicity of BVDV in pregnant goats. Except for reproductive disorders, clinical manifestation of experimentally infected does showed pyrexia following inoculation of virus indicating presence of virus in blood (viraemia). A parallel relationship between degree of viraemia and rectal temperature was recorded by Walz et al. (2001) who added that degree of viraemia induced during BVDV infection is associated with severity of clinical disease. Profuse watery diarrhea was observed in the inoculated does with NADL strain, while mild and intermittent diarrhea was seen in inoculated does with camel strain. The occurrence of diarrhea could be explained on basis of intestinal mal absorption as a result of desquamation of absorptive epithelium lining of villi during enteritis. Malabsorptive diarrhea commonly result

In the current work, inoculation of BVDV either NADL or camel strain induced vacuolization of hepatic cells, multiple foci of hepatic cell necrosis associated with mononuclear cell infiltration. Meanwhile, in lungs multiple areas of alveolar emphysema associated with areas of chronic interstitial pneumonitis were observed. Similar results were recorded in experimentally infected calves with BVDV type 1 by Ellis et al. (1998); Baule et al. (2001) and Galav et al. (2007). Recently, Glotov et al. (2016) demonstrated the pathogenicity and virulence of the Russian BVDV strains of subtypes (1a, 1b, and 1d) for 4-6 month old calves developed signs of respiratory disease and diarrhea, in addition to macroscopic changes in respiratory organs and intestine.

Virus genome levels were also detected by RT-PCR in liver and lung which increased only late after experimental infection of calves with genotype 1 strain that confirms the secondary role of these organs in BVD. However, the increased levels of virus in the lung at final stages of the infection could influence in the appearance of bovine respiratory diseases because of the capacity of BVDV for enhancing susceptibility to secondary infections with potential respiratory tract pathogens such as Parainfluenza -3 (PI3). Bovine herpes virus1 (BHV-1) or pasturella hemolytica that often lead to pneumonia attributed to local and/or general immunosuppression of virus (Baule et al., 2001; Fulton et al., 2002 and Pedrera et al., 2012). In connection with this, alveolar macrophages functions were significantly reduced following BVDV infection (Welsh et al., 1995).

Concerning the effect of BVDV either camel or NADL strain on kidney, the histopathological picture was characterized by hypercellularity of glomerular tuft with adhesion to parietal layer of
Bancroft, J.D., Baker, J.C., 1995. Immunofluorescent technique. Developed in lymphatic organs. Viral antigen was also identified within the various tissues by addition to its adverse effect on reproductive performance. Moreover, severe lymphoid depletion developed in lymphatic organs. Viral antigen in kidney proved nephrotropic nature of the virus and virus –induced glomerulonephritis (Galav et al., 2007).

The histopathological picture of lymphoid tissues in the present study revealed marked lymphocytic cell depletion of lymph nodes, Peyer’s patches and spleen, in addition to detection of viral antigen within the tissues. These findings were previously recorded in calves experimentally infected with BVDV by Ellis et al. (1998); Baule et al. (2001); Liebler-Tenorio et al. (2002&2004); Galav et al. (2007); Raizman et al. (2011) and wang et al. (2014). The generalized infection of lymphoid tissues is consistent with the lymphotropic nature of BVDV (Baule et al., 2001). In the acutely infected calves depletion of lymphoid tissues was seen at 6, 9, and 13 days (PI) and viral antigen was widespread in lymphoid tissues at 6 days PI but had been mostly eliminated at 9 and 13 days PI (Liebler-Tenorio et al., 2004). In this respect, it has been reported that cytopathogenic BVDV localizes in the germinal centers of lymph nodes (Fray et al., 2000), tonsils, and gut associated lymphoid tissue of Peyer’s patches before spreading to gastrointestinal epithelium (Liebler-Tenorio et al., 2002). The highest viral genome loads were recorded at 9 days PI. In tonsils, ileal lymph nodes, distal ileum and spleen of infected calves, showing the main role of these secondary lymphoid organs in the pathogenic mechanisms of BVDV (Pedrera et al., 2012). The pathological changes of lympho-reticular tissue in the present work support to an assumption that virus may cause immunosuppression and enhancing susceptibility for secondary infection. Immunosuppression is associated with direct effects of BVDV on circulating T and B lymphocytes (Bolín et al., 1985) and apoptosis of lymphocytes in gut associated lymphoid tissue (Pedrera et al., 2012). It has been found that up to 85% of BVDV infected animals also were bacteremic which support immunosuppression as being a manifestation of infection with virus. (Reggiardo and Kaeberle, 1981). Cytopathogenic BVDV also promotes monocyte activation and differentiation, as well as inhibiting Ag presentation to T cells. This leads to inflammation, viraemia and impairing antiviral defenses (Lee et al., 2009).

The intestinal lesions of both infected groups in the current work were primarily inflammatory in nature and characterized by desquamation of epithelium lining of mucosa, highly infiltration of oedematous lamina propria with mononuclear cells, in addition to mucous degenerative changes of epithelium lining of intestinal crypts. These findings were in agreement with those in experimentally infected calves by Ellis et al. (1998); Baule et al. (2001) and Galav et al. (2007). BVDV had an affinity for and a direct necrotizing effect on the epithelial cell lining the lower alimentary tract (Ruth, 1986). It is noteworthy that there was an increase in the number of globule leukocytes in the epithelium of crypts. This finding was in parallel line with observation of Wilhelmsen et al. (1990) and Baule et al. (2001) who noticed presence of scattered globule leukocytes infiltration in mesenteric lymph nodes, Peyer’s patches, ileocecal junction and the intestinal submucosa of inoculated calves with BVDV. In this context, Jubb et al. (1985) reported that globule leukocytes appeared as mononuclear cells with large, eosinophilic cytoplasmic granules, they possibly were derived from intestinal mast cells. The effects of histamine, serotonin and other mediators released by mast cells on vascular tone and permeability, motility chemotaxis and effect or function of leukocytes and possible in mucous release were many and complex. It is evident that these cells have important role in the immune response against BVDV.

It could be concluded from the present study that experimental infection with BVDV either camel or NADL strain in pregnant goats induced pronounced histopathological changes in visceral organs, in addition to its adverse effect on reproductive performance. Moreover, severe lymphoid depletion developed in lymphatic organs. Viral antigen was also identified within the various tissues by immunofluorescent technique.

References


