Archives of Razi Institute, Vol. 72, No. 4 (2017) 255-263

Original Article

Clinical, hematologic, and biochemical findings in cattle infected with lumpy skin disease during an outbreak in southwest Iran

Jalali [1, *], S.M., Rasooli [1, 2], A., Seifi Abad-Shapouri [3], M.R., Daneshi [4], M.

1. Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
2. Department of Animal Health Management, School of Veterinary Medicine, Shiraz University, Shiraz, Iran
3. Department of Pathobiology, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran
4. DVM Graduate, Faculty of Veterinary Medicine, Shahid Chamran University of Ahvaz, Ahvaz, Iran

Received 29 June 2016; accepted 29 October 2016
Corresponding Author: mi.jalali@scu.ac.ir

ABSTRACT

This study was performed to determine the clinical, hematologic, and biochemical findings in animals affected with lumpy skin disease (LSD) in southwest Iran. Sixty cattle with LSD were included in this study and compared with 20 healthy ones as the control group. The disease was diagnosed based on clinical examination and confirmed by polymerase chain reaction analysis of the blood samples. The major observed clinical signs included skin nodules, fever, enlarged lymph nodes, and edema. In hematologic assessment, the average numbers of leukocytes, lymphocytes, eosinophils, erythrocytes, and platelets, as well as the average level of hemoglobin in the infected animals were significantly lower than in the control group. Biochemical experiments showed that the serum glucose, total and direct bilirubin, aspartate aminotransferase, and creatine phosphokinase activities in the infected group were significantly elevated. LSD also caused a significant reduction in the levels of serum creatinine, albumin, and iron. In total, LSD was associated with an overall decline in different blood cell types and significant changes in serum biochemical profile. These alterations could be related to the inflammatory disease processes and injuries in various organs, especially the liver. Hematologic and biochemical profiles can be utilized to better understand different aspects of LSD pathogenesis and ultimately improve its prognostic, management, and treatment methods.

Keywords: Lumpy skin disease, Clinical signs, Hematology, Biochemistry, Iran

Analyse des résultats cliniques, hématologiques et biochimiques chez les bovins d'élevage atteints de dermatose nodulaire contagieuse lors d'une épidémie dans le sud-ouest de l'Iran

Résumé: Cette étude a été réalisée dans l'objectif d'étudier les signes cliniques, les résultats hématologiques et biochimiques chez les bovins d'élevage atteints de dermatose nodulaire contagieuse lors d'une épidémie dans le sud-ouest de l'Iran. Un total de 60 bovins soufrantde dermatose nodulaire contagieuse ont été envoyés à l'hôpital vétérinaire de l'université Shahid Chamran d'Ahvaz alors que20 bovins en bonne santé constituaient le groupe témoin. Le diagnostic de la maladie a été effectué sur la base d'examens cliniques,suivi par la confirmation du diagnostic parPCR sur les 'échantillons sanguins. Parmi les symptômes cliniques observés chez les bovins malades, on peut citer notamment les nodules de la peau, la fièvre, les ganglions lymphatiques et l'œdème. Lors des analyses hématologiques , le nombre moyen de leucocytes, de lymphocytes, d'éosinophiles, d'érythrocytes, d'hémoglobine et de plaquettes chez les animaux infectés était significativement plus faible que le groupe témoin. Les tests biochimiques, ont révélé que les taux de glucose, de bilirubine totale et directe. De plus, le

niveau d'activité des enzymes AST et Cpk dans le groupe infecté état significativement plus élevécomparé augroupe sain. Une diminution significative du taux de créatinine, d''albumine et de fer a été également observée chez les bovins atteints de dermatose nodulaire contagieuse. Dans l'ensemble, l'incidence de la dermatose nodulaire contagieuse chez les bovins était associée à une diminution du nombre total de cellules dans les différents groupes sanguins (Pancytopénie) et à des changements significatifs dans les profils biochimiques du sérum. Ces changements peuvent être liés au processus inflammatoire de la maladie et aux dommages systémiques créés dans divers organes, tel que le foie. L'analyse du profil sanguin et biochimique du lymphœdème provenant des animaux atteints de dermatose nodulaire contagieuse s'est avérée utile dans l'identificationdes différents aspects de la pathogenèse de la maladie et finalement pour évaluer le pronostic et améliorer les méthodes de contrôle et de traitement.
Mots-clés: dermatose nodulaire contagieuse, signes cliniques, hématologie, biochimie, Iran

INTRODUCTION

Lumpy skin disease (LSD) is a highly contagious viral disease of cattle, which is associated with huge economic losses in the livestock industry. The disease is characterized by fever, firm circumscribed skin nodules, necrotic plaques in the mucosal membranes, especially in the upper respiratory tract, generalized lymphadenitis, mastitis, orchitis, anorexia, and even death (Prozesky and Barnard, 1982; Coetzer, 2004) .

The disease is caused by a virus belonging to the *Poxviridae* family, genus *Capripoxvirus*. This virus has strong resemblance to sheep and goat pox viruses such that they cannot be differentiated serologically but are genetically dissimilar (Maclachlan and Dubovi, 2010). Arthropods play a major role in the mechanical transmission of LSD virus, but direct contact with the skin lesions, saliva, nasal discharge, milk, or semen of infected animals are also the possible routes of disease transmission. The disease morbidity varies between 5% and 45% depending on the population of vector insects and sensitivity and breed of at-risk animals (Salib and Osman, 2011). However, LSD mortality is low and rarely exceeds 1-3% (Coetzer, 2004). The disease was first reported in 1929 in Zambia, and subsequently, many epidemics in South Africa and most African countries led to the involvement of a large number of animals (Tuppurainen and Oura, 2012). LSD was observed in the Middle East in 1989 and since then several outbreaks have occurred, and there is a risk of LSD becoming endemic in some countries in the region (Oie, 2010). In Iran, LSD was first reported in June 2014 in Kurdistan Province (Oie, 2014) and was spread across several regions including Khouzestan province.

Considering the rapid and widespread transmission and serious complications of LSD, detailed examination of various aspects of the disease is essential for better understanding the disease pathogenesis, early diagnosis, appropriate treatment, and preventive measures. In view of scarcity of information regarding the laboratory changes in LSD and recent outbreaks of the disease in southwest Iran, this study was performed to determine the hematologic and serum biochemical findings in association with clinical signs in LSD-affected cattle in Ahvaz, southwest Iran.

MATERIALS AND METHODS

Animals. The present study was conducted in Ahvaz, Khouzestan province, a tropical area located in southwest of Iran, where an outbreak of LSD occurred during July-December 2014. Sampling was carried out from October to December 2014. Sixty mixed-breed native cattle with the clinical signs of LSD (LSD group) that were brought to the veterinary teaching hospital of Shahid Chamran University of Ahvaz were included in this study. This group comprised of 12 males and 48 females, which ranged in age from 1 to 5 years old. The disease was diagnosed based on clinical examination and laboratory confirmation by polymerase chain reaction (PCR) analysis of the blood samples. Twenty clinically healthy cattle were also

sampled during the same period as the control group with 4 male and 16 female animals aged between 9 months and 6 years.

Clinical examination. Physical examination of all the studied animals was performed considering the general and specific clinical signs of LSD. Signalments and signs of each animal, comprising of sampling time, age, sex, body temperature, anorexia, skin nodules, superficial lymphadenopathy, and edema, were recorded.

Blood sampling. Blood samples were collected from the jugular veins into anticoagulant (EDTA) containing and plain tubes. Serum and whole blood samples (after hematologic examination) were stored at -70 °C until further laboratory assessment.

PCR analysis. DNA was extracted using a genomic DNA purification kit (Cinna Gen, Iran). A PCR method was employed to specifically identify *Capripoxvirus* based on Oie's recommended method, which was previously explained by Ireland and Binepal (1998). Concisely, one pair of primers based on the viral attachment protein encoding gene sequence of *Capripoxvirus* was utilized to amplify virus DNA. The primers were forward strand primer 5′- TCC-GAG-CTC-TTT-CCT-GAT-TTT-TCT-TAC-TAT -3′ and reverse strand primer 5′- TAT- GGT-ACC-TAA-ATT-ATA-TAC-GTA-AAT-AAC-3′, yielding a 192 bp product. PCR was carried out in a total reaction volume of 50 µl containing 25 µl of 2× PCR Master Mix (Amplicon, Denmark) and 25 pmol of each primer; further, 5 µl of DNA suspension was used as template in the PCR reaction. The amplification was performed in a thermocycler (Eppendorf, Germany) under the following program: an initial denaturation step at 94 °C for 2 min followed by 40 cycles at 94 °C for 45 s (denaturing step), 50 °C for 50 s (annealing step), and 72 °C for 60 s (extension step) with a final extension step at 72 °C for 2 min. PCR products were electrophoresed on 1.5% agarose gel stained by SafeStain (CinnaGen Inc., Iran) and the results were visualized by ultraviolet transilluminator.

Hematologic assessment. Hematologic parameters including total erythrocyte count (RBC), hematocrit value (HCT), hemoglobin concentration (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH), mean corpuscular hemoglobin concentration (MCHC), and total white blood cells (WBC) were determined by the BC-2800Vet hematology analyzer (Mindray, China). Differential leukocyte counts were also estimated manually.

Biochemical analysis. Serum biochemical parameters including total protein, albumin, glucose, urea, creatinine, iron, total and direct bilirubin concentrations, aspartate aminotransferase (AST), alkaline phosphatase (ALP), and creatine phosphokinase (CPK) activities were assessed using a biochemistry autoanalyser (BT-1500, Biotechnica, Italy) and Parsazmun kits (Iran).

Statistical analysis. Independent samples t-test, analysis of variance (ANOVA), and Tukey's Post hoc tests were employed to compare laboratory-obtained values between the groups using SPSS, version 16. All the values were expressed as mean and standard error (SE), and p-values less than 0.05 were considered statistically significant.

RESULTS

Clinical signs and characteristics. The apparent clinical signs including anorexia, reduced lactation, fever, skin nodules, enlarged lymph nodes, and edema were observed in cattle with LSD (LSD group; Table 1).

Table 1. Clinical signs in cattle with lumpy skin disease (n=60)

Clinical signs	Frequency	Percentage
Skin nodules	59	98.33
Lymph nodes enlargement	59	98.33
Fever (39.5°C<)	35	58.33
Anorexia	50	83.33
Reduced lactation (in lactating cows, n=24)	23	95.83
Edema	26	43.33
Mucosal hyperemia	10	16.66
Corneal opacity	4	6.66
Conjunctivitis	5	8.33
Respiratory involvement	2	3.33

Skin nodules were distributed in various body parts involving the neck, chest, abdomen, udder, limbs, perineal area, muzzle, and in some cases, all over the body. In some affected cattle, nodules ended in necrosis, secondary infections, or myiasis. Superficial (prescapular and prefemoral) lymph nodes were enlarged in most cases. Edema was observed in the eyelids, mandibular and neck area, ventral thorax, perineal area, udder, and limbs. Increased ocular and nasal discharge, excessive salivation, pneumonia, conjunctivitis, and corneal opacity were also among the symptoms of the disease in some cases (figures 1, 2).

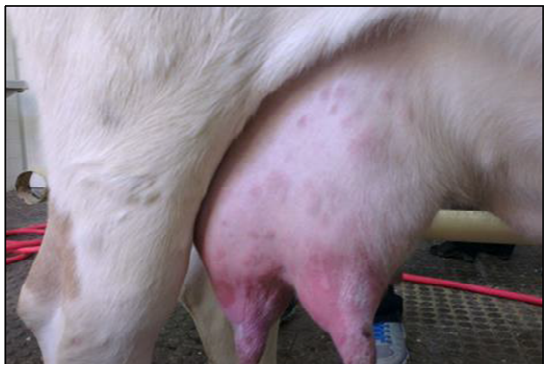

Figure 1. Nodules in the hind limb and udder skin of a cattle

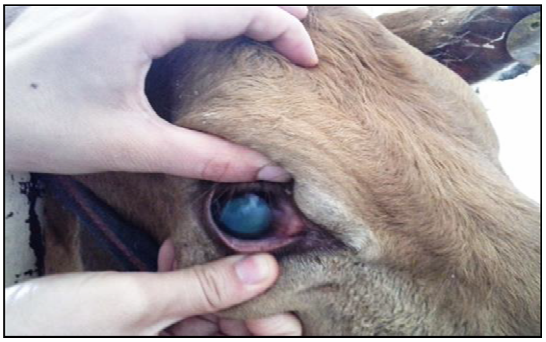

Figure 2. Conjunctivitis and corneal opacity in a cattle with clinical lumpy skin disease

PCR confirmation. *Capripoxvirus* infection was confirmed by the PCR analysis of blood samples and amplification of a 192 bp DNA fragment in all the symptomatic cattle (Figure 3).

Hematologic and biochemical assessments. Hemogram analysis revealed that total leukocyte count (WBC), lymphocytes (lymph), and eosinophils (Eos) were significantly decreased in the LSD group compared to the control group (P< 0.05; Table 2).

Table 2. Hematological results as mean ± SE in the control and lumpy skin disease groups

	Control group	LSD group	P value
WBC (×10^3/uL)	10.15 ± 0.51	7.06 ± 0.50	0.00
Neut (×10^3/uL)	2.62 ± 0.28	2.96 ± 0.30	0.54
Lymph (×10^3/uL)	7.29 ± 0.48	3.87 ± 0.31	0.00
Mon (×10^3/uL)	0.03 ± 0.01	0.02 ± 0.00	0.60
Eos (×10^3/uL)	0.20 ± 0.04	0.06 ± 0.01	0.00
RBC (×106/uL)	7.20 ± 0.39	6.14 ± 0.19	0.01
Hb (g/dL)	8.21 ± 0.26	7.24 ± 0.20	0.01
HCT (%)	30.00 ± 0.86	28.44 ± 0.82	0.30
MCV (fL)	42.96 ± 1.38	47.34 ± 1.14	0.04
MCH (pg)	11.67 ± 0.36	11.99 ± 0.29	0.55
MCHC (g/dL)	27.29 ± 0.24	25.43 ± 0.13	0.00
RDW (%)	17.51 ± 0.40	17.17 ± 0.25	0.50
PLT (×10^3/uL)	437.30 ± 3.84	249.88 ± 14.70	0.00

WBC: white blood cells RBC: total erythrocyte count
HCT: hematocrit value MCV: mean corpuscular volume
MCHC: mean corpuscular hemoglobin concentration
MCH: mean corpuscular hemoglobin
RDW: red cell distribution width
PLT: platelets

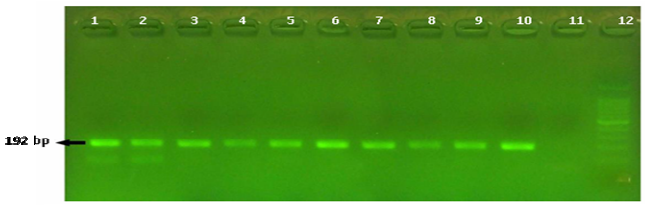

Figure 3. Agarose gel electrophoresis of *Capripoxvirus* polymerase chain reaction-amplified fragments. Lane 1-9: infected samples, lane 10: *Capripoxvirus* positive control, lane 11: Negative control, and lane 12: DNA size marker

In addition, there was a significant decline in RBC, Hb, and MCHC of the diseased cattle (P<0.05). HCT in the LSD group was also reduced, although this alteration was not statistically significant compared to the control group (P>0.05). In contrast, MCV was significantly higher in the diseased animals than in the healthy ones (P<0.05). Moreover, a reduction was observed in platelet count in the LSD group to about half of that in the control group (P<0.05). Serum biochemical analysis showed a significant decrease in creatinine and albumin concentrations (P<0.05); however, the amount of total serum protein remained unchanged in the LSD group compared to the control group (Table 3).

Table 3. Serum biochemical results as mean ± SE in the control and LSD groups

	Control group	LSD group	P-value
Urea (mg/dl)	34.15 ± 0.68	33.54 ± 0.87	0.69
Creatinine (mg/dl)	1.47 ± 0.05	1.13 ± 0.02	0.00
Glucose (mg/dl)	72.10 ± 1.97	86.80 ± 4.13	0.04
Albumin (g/dl)	3.72 ± 0.06	3.31 ± 0.04	0.00
Protein (g/dl)	7.66 ± 0.14	7.89 ± 0.14	0.40
ALP (U/l)	237.94 ± 36.24	194.22 ± 14.17	0.17
CPK (U/l)	232.26 ± 22.21	460.73 ± 56.49	0.02
Bilirubin total (mg/dl)	0.52 ± 0.00	1.04 ± 0.04	0.00
Bilirubin direct (mg/dl)	0.13 ± 0.00	0.24 ± 0.01	0.00
AST (U/l)	68.90 ± 2.95	173.50 ± 18.15	0.00
Iron (µg/dl)	92.75 ± 8.77	36.36 ± 3.85	0.00

AST: aspartate aminotransferase
CPK: creatine phosphokinase ALP: alkaline phosphatase

Serum glucose, total and direct bilirubin concentrations, and the activity of AST and CPK enzymes were significantly elevated in the diseased group (P<0.05). There was also a significant reduction in serum iron in the cattle with LSD in contrast to the healthy ones (P<0.05). LSD course was divided into three assumed stages according to the time elapsed since the onset of clinical signs. The disease stages included the early (1 to 3 days of clinical signs), mid (4 to 7 days), and late (8 to 14 days) stages. Hematologic and biochemical data in the cattle at each stage were then compared with those of the control group. Comparison of hematologic profiles in cattle in different LSD stages showed that the WBC and lymphocyte counts were significantly reduced in the first week of the disease (P<0.05), while they were increased in the second week (Table 4).

Table 4. Hematological results as mean ± SE in the control and lumpy skin disease groups based on disease stage.

		LSD groups		
	Control n=20	Early stage (1- 3 days) n=17	Mid stage (4-7 days) n=24	Late stage (8-14 days) n=12
WBC($\times10^3$/uL)	10.15 ± 0.51 ^{a*}	6.71 ± 0.81 ^{b}	6.13 ± 0.62 ^{b}	8.73 ± 1.40 ^{ab}
Neut ($\times10^3$/uL)	2.62 ± 0.28	2.44 ± 0.46	2.50 ± 0.42	3.69 ± 0.57
Lymph ($\times10^3$/uL)	7.29 ± 0.48 ^{a}	3.62 ± 0.34 ^{b}	3.55 ± 0.83 ^{b}	4.96 ± 1.12 ^{b}
Mon ($\times10^3$/uL)	0.03 ± 0.01	0.02 ± 0.01	0.03 ± 0.01	0.01 ± 0.00
Eos ($\times10^3$/uL)	0.20 ± 0.04 ^{a}	0.09 ± 0.05 ^{ab}	0.04 ± 0.02 ^{b}	0.05 ± 0.03 ^{ab}
RBC ($\times10^6$/uL)	7.20 ± 0.39	6.21 ± 0.43	6.35 ± 0.32	6.16 ± 0.33
Hb (g/dL)	8.21 ± 0.26	7.52 ± 0.48	7.36 ± 0.32	6.86 ± 0.37
HCT(%)	30.00 ± 0.86	29.85 ± 1.94	28.69 ± 1.23	27.22 ± 1.49
MCV(fL)	42.96 ± 1.38	48.85 ± 2.10	46.26 ± 1.78	44.98 ± 2.53
MCH(pg)	11.67 ± 0.36	12.21 ± 0.52	11.80 ± 0.46	11.28 ± 0.62
MCHC(g/dL)	27.29 ± 0.24 ^{a}	25.13 ± 0.24 ^{b}	25.59 ± 0.13 ^{b}	25.20 ± 0.30 ^{b}
RDW(%)	17.51 ± 0.40	16.56 ± 0.44	17.70 ± 0.39	17.45 ± 0.67
PLT($\times10^3$/uL)	437.30 ± 30.84 ^{a}	254.87 ± 32.06 ^{b}	252.00 ± 23.88 ^{b}	229.30 ± 19.64 ^{b}

WBC: white blood cells RBC: total erythrocyte count
HCT: hematocrit value MCV: mean corpuscular volume
MCHC: mean corpuscular hemoglobin concentration
MCH: mean corpuscular hemoglobin RDW: red cell distribution width
PLT: platelets

There was also a decline in eosinophil count in all the disease stages, which was significant during the mid-stage (4 to 7 days; P<0.05). Means of RBC, Hb, HCT, and MCHC were reduced throughout the course of the disease, with the lowest values were obtained in the late stage. However, these changes, except in MCHC, were not statistically significant compared to the control group (P>0.05). Significant thrombocytopenia was a constant finding during the whole disease period (P<0.05). Serum biochemical analysis in the cattle with LSD in different stages revealed a persistent decrease in creatinine and iron levels compared to the control group (P<0.05; Table 5). Serum albumin concentration was also reduced across all the disease stages, which was statistically significant from the fourth day onwards when compared with the healthy cattle (P<0.05). A significant rise in CPK and AST enzyme activities and the levels of total and direct bilirubin was observed in all the diseased cattle of any stage (P<0.05).

Table 5. Serum biochemical results as mean ± SE in control and lumpy skin disease groups based on disease stage

		LSD groups		
	control n=20	Early stage (1- 3 days) n=17	Mid stage (4-7 days) n=24	Late stage (8-14 days) n=12
Urea (mg/dl)	34.15 ± 0.68	32.93 ± 1.18	33.91 ± 0.94	35.36 ± 3.53
Creatinine (mg/dl)	1.47 ± 0.05 [a]	1.19 ± 0.05 [b]	1.05 ± 0.04 [b]	1.16 ± 0.07 [b]
Glucose (mg/dl)	72.10 ± 1.97	83.87 ± 5.20	93.87 ± 8.24	76.46 ± 7.03
Albumin (g/dl)	3.72 ± 0.06 [a]	3.47 ± 0.09 [ab]	3.27 ± 0.08 [b]	3.20 ± 0.11 [b]
Protein (g/dl)	7.66 ± 0.14	8.00 ± 0.21	7.84 ± 0.24	7.48 ± 0.34
ALP (U/l)	237.94 ± 36.24	196.62 ± 27.98	183.83 ± 14.55	210.15 ± 37.59
CPK (U/l)	232.26 ± 22.21	544.56 ± 123.93	411.87 ± 72.21	606.81 ± 151.95
Bilirubin total (mg/dl)	0.52 ± 0.00 [a]	0.97 ± 0.37 [b]	1.05 ± 0.24 [b]	1.22 ± 0.56 [b]
Bilirubin direct (mg/dl)	0.13 ± 0.00 [a]	0.22 ± 0.01 [b]	0.27 ± 0.01 [b]	0.24 ± 0.02 [b]
AST (U/l)	68.90 ± 2.95 [a]	135.11 ± 30.50 [ab]	176.25 ± 23.80 [b]	195.46 ± 40.09 [b]
Iron (µg/dl)	92.75 ± 8.77 [a]	32.81 ± 5.46 [b]	31.27 ± 5.22 [b]	49.50 ± 10.86 [b]

* Dissimilar letters in each row indicate significant difference between groups.
AST: aspartate aminotransferase
CPK: creatine phosphokinase ALP: alkaline phosphatase

DISCUSSION

LSD, an endemic poxvirus disease of cattle in Africa, recently reached the Middle East, including Iran, where it was associated with several outbreaks and heavy economic losses. In the present study, disease diagnosis was based on clinical signs that were confirmed by PCR detection of *Capripoxvirus* infection. On clinical examination of the cattle suffering from LSD, skin nodules, superficial lymph node enlargement, and loss of appetite were the most frequent symptoms. Other signs included fever, edema in various body parts, and mucosal discharge. A large number of studies have documented the same symptoms in natural (Agag et al., 1992; Body et al., 2012; El-Neweshy et al., 2013) or experimental infections (Osuagwuh et al., 2007). Fever is usually the first noticeable sign of LSD that can take 4 to 14 days. Prolonged fever is probably associated with secondary bacterial infections (Agag et al., 1992; Coetzer and Tustin, 2004). As the disease progresses, skin nodules become necrotic and some form deep scabs that will be removed from the skin and provide suitable conditions for bacterial contamination or myiasis (Ahmed and Zaher, 2008; Body et al., 2012). Hematologic assessment of the blood samples obtained from cattle with LSD revealed a decrease in various leukocyte types, lymphocytes, and eosinophils in particular, and erythrocytes (pancytopenia) in comparison with the healthy ones. Various hematologic test results were recorded by Abutarbush (Abutarbush et al., 2016) in LSD with some animals showing leukocytosis and others leukopenia. Most of the diseased cattle were also anemic with decreased HCT, MCH, and MCV. Reduced proliferation of different hematopoietic cell lines is a temporary finding in many subclinical or acute viral diseases. Leukopenia observed in the initial

phases of acute infectious diseases in ruminants is also associated with increased tissue demand and neutrophil margination. In addition, lymphopenia is a more frequent finding in viral infections than in bacterial ones. Generalized distribution of antigens in systemic infectious diseases results in lymphopenia, which is due to lymph node sequestration of peripheral blood lymphocytes (Latimer, 2011). In the current study, reduced erythrocyte counts, HCT, Hb, and MCHC in the cattle suffering from LSD may be considered as anemia of inflammation. This type of anemia is caused by inflammatory cytokines, including TNF, IL-1α, IL-1β, and IF-γ, lower bone marrow responsiveness to erythropoietin. Anorexia and simultaneous decrease in serum iron can also play a role in the development of anemia (Morceau et al., 2009; Latimer, 2011). Platelet count in the LSD-infected cattle was significantly lower than in the healthy controls, which was in agreement with Abutarbush (Abutarbush, 2015)findings. Thrombocytopenia may be the result of decreased platelet production in the bone marrow or sequestration of platelets due to splenomegaly (Morris, 2002). Considering vasculitis and vascular thrombosis as the key histopathologic features of the disease, it can also be considered as one of the main causes of thrombocytopenia, which occurred in clinical *Capripox* infection in this study (Coetzer and Tustin, 2004; Tageldin et al., 2014; Abutarbush et al., 2016). Serum biochemical analysis in the LSD group showed a significantly lower creatinine concentration than in the control group, which can be attributed to anorexia and loss of muscle mass. Although in clinical lumpy skin decreased serum creatinine was found by Abutarbush (Abutarbush, 2015; Abutarbush et al., 2016), other researchers recorded a rise in serum urea and creatinine as a result of renal degenerative changes (Agag et al., 1992; Hassan et al., 2011). This discrepancy may be in part due to the differences in disease stage, breed, and body condition. Decreased serum albumin with no significant change in total protein in the diseased group may reflect anorexia and hepatic parenchymal injury along with increased serum globulin in the form of immunoglobulin and acute-phase proteins due to immune responses. These results were consistent with earlier documented data (Agag et al., 1992; Ahmed and Zaher, 2008; Hassan et al., 2011). Serum glucose concentration was elevated in clinically *Capripox* infected cattle compared to uninfected ones that may be related to increased levels of endogenous corticosteroids during the course of the disease (Evans and Duncan, 2003). There were also rises in serum AST activity and total and direct bilirubin levels in the LSD group, which indicate possible hepatocyte and bile duct damage due to viral pathogens. Degenerative histopathologic changes in the liver, elevated hepatic enzyme activity, and bilirubin concentration in LSD were documented before (Agag et al., 1992; Hassan et al., 2011). Increased CPK together with AST activity may be a sign of skeletal and cardiac muscle injuries in the LSD group, which is in agreement with the findings of other researchers who recorded histopathologic changes in the heart, muscle fibers, lymph nodes, and skin (Prozesky and Barnard, 1982; Woods, 1988). Serum iron assessment in this study revealed a significant reduction in the LSD-involved group compared to the control group that was comparable to other previous findings (Agag et al., 1992; Ahmed and Zaher, 2008). Chronic inflammatory diseases, release of cytokines and inflammatory mediators, and malnutrition are considered as possible causes of hyposideremia. In addition, studies have shown that many viral infections can affect iron metabolism and regulation in the body (Drakesmith and Prentice, 2008). No significant changes were observed in hematologic or biochemical results among cattle examined in diverse stages of LSD course. It seems that clinical signs and hematologic and biochemical profiles remain relatively constant within two weeks from the beginning of the disease. This marks the continuance of the acute phase of the disease and its pathogenesis due to *Capripoxvirus* itself or bacterial infections. Improvement in clinical and laboratory signs and

recovery probably occur over time. In this study, due to lack of access to a sufficient number of LSD-affected animals, it was not possible to compare the results in the subsequent weeks. However, our results were consistent with those of Agag et al. (1992). Their study showed that fever, as the first clinical symptom, lasted up to 14 days and, in some cases, even for 21 days. Furthermore, analysis of some serum biochemical parameters and enzyme activities revealed changes within 14 to 21 days followed by improvement.

In brief, LSD in cattle was accompanied with an overall reduction in the number of erythrocytes, various leukocyte types (pancytopenia), and significant changes in the serum biochemical profile, especially in hepatic enzyme activities and albumin and glucose concentrations. These alterations can be explained by the inflammatory response and systemic pathogenesis in different body organs due to *Capripoxvirus* infection. It can be concluded that hematologic and serum biochemical assessments can provide valuable information on the severity of pathogenesis and prognosis of the disease.

Ethics

I hereby declare all ethical standards have been respected in preparation of the submitted article.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgements

The authors would like to thank the Deputy of Research of Shahid Chamran University of Ahvaz for financial support of the research project, no-9158794. We also acknowledge all the veterinarians and technicians in the Faculty of Veterinary Medicine who helped us with sample collection.

References

Abutarbush, S., Hananeh, W., Ramadan, W., Al Sheyab, O., Alnajjar, A., Al Zoubi, I., *et al.*, 2016. Adverse reactions to field vaccination against lumpy skin disease in Jordan. Transbound Emerg Dis 63.

Abutarbush, S.M., 2015. Hematological and serum biochemical findings in clinical cases of cattle naturally infected with lumpy skin disease. J Infect Dev Ctries 9, 283-288.

Agag, B., Mousa, S., Hassan, H., Saber, M., El-Deghidy, N.S., El-Aziz, A.M.A., 1992. Clinical, serological and biochemical studies on lumpy skin disease. J APPL ANIM RES 1, 13-23.

Ahmed, W., Zaher, K.S., 2008. Observations on lumpy skin disease in local Egyptian cows with emphasis on its impact on ovarian function. Afr J Microbiol Res 2, 252-257.

Body, M., Singh, K.P., Hussain, M.H., Al-Rawahi, A., Al-Maawali, M., Al-Lamki, K., *et al.*, 2012. Clinico-histopathological findings and PCR based diagnosis of lumpy skin disease in the Sultanate of Oman. Pak. Vet. J 32, 206-210.

Coetzer, J., 2004. Lumpy skin disease. Infectious diseases of livestock 2, 1268-1276.

Coetzer, J., Tustin, R., 2004. Infectious diseases of livestock. Volume Three, Oxford University Press.

Drakesmith, H., Prentice, A., 2008. Viral infection and iron metabolism. Nat Rev Microbiol 6, 541-552.

El-Neweshy, M., El-Shemey, T., Youssef, S., 2013. Pathologic and immunohistochemical findings of natural lumpy skin disease in Egyptian cattle. Pak Vet J 33, 60-64.

Hassan, H., El-Kirdasy, A., Ali, M., 2011. Immunobiochemical profile in cattle infected with lumpy skin disease. J. Basic Appl. Chem 1, 21-25.

Latimer, K.S., 2011. Duncan and Prasse's veterinary laboratory medicine: clinical pathol, John Wiley & Sons.

Maclachlan, N.J., Dubovi, E.J., 2010. Fenner's veterinary virology, Academic press.

Morceau, F., Dicato, M., Diederich, M., 2009. Pro-inflammatory cytokine-mediated anemia: regarding molecular mechanisms of erythropoiesis. Mediators Inflamm 2009.

Osuagwuh, U.I., Bagla, V., Venter, E.H., Annandale, C.H., Irons, P.C., 2007. Absence of lumpy skin disease virus in semen of vaccinated bulls following vaccination and subsequent experimental infection. Vaccine 25, 2238-2243.

Prozesky, L., Barnard, B., 1982. A study of the pathology of lumpy skin disease in cattle. Onderstepoort J Vet Res 49, 167-175.

Salib, F.A., Osman, A.H., 2011. Incidence of lumpy skin disease among Egyptian cattle in Giza Governorate, Egypt. Vet World 4.

Tageldin, M.H., Wallace, D.B., Gerdes, G.H., Putterill, J.F., Greyling, R.R., Phosiwa, M.N., *et al.*, 2014. Lumpy skin disease of cattle: an emerging problem in the Sultanate of Oman. Trop Anim Health Prod 46, 241-246.

Tuppurainen, E., Oura, C.A., 2012. lumpy skin disease: an emerging threat to Europe, the Middle East and Asia.Transbound Emerg Dis 59, 40-48.

Woods, J., 1988. Lumpy skin disease—a review. Trop Anim Health Prod 20, 11-17.