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CLINICAL AND LABORATORY STUDIES OF FACIAL ECZEMA SYNDROME IN LOCAL SHEEP BREEDS OF BASRAH GOVERNORATE

*Kamal M. Alsaad , *Hassanin.H.N.AL Autaish, **Jihad Abdulameer Ahmed
*Department of internal and preventive medicine,**Department of pathology and poultry diseases
College of Veterinary Medicine, University of Basrah, Basrah, Iraq

ABSTRACT

The study was carried out on 523 local sheep breeds of different ages and of both sexes represents different herds, reared in different areas of Basrah governorate. Fifty four(54) local sheep breeds were show different clinical sings including sings of photosensitization, parakeratosis , alopecia, Intense itching ,swelling of ears, anorexia and decreased milk production and twenty three(23) clinically healthy local sheep breeds were considered as controls. The study was documented at late summer and early autumn time / 2015. Complete clinical examinations had been applied to all animals. Results indicated that diseased sheep show signs of anorexia, salivation, decrease milk production in milking animals, transient diarrhea, hypotricosis specially of face with irregular patches of wool looseness, Intense itching of different body parts, signs of parakeratosis, swelling and dropping of ears, icteric mucous membranes specially of eyes, furthermore, on clinical examinations diseased animals show rapid abdominal respiration, tachycardia with strong heart beats, decrease ruminal contractions and increase body temperature, moreover hematological examinations show significant decrease in total RBC, Hb and PCV count reflecting Macrocytic hypochromic anemia, moreover total leukocytes count were also increased significantly due to increase lymphocytes and eosinophiles. Data concerning biochemical analysis revealed significantly decrease in total protein values and zinc, whereas ALT.AST.ALP. Total and direct bilirubine and GGT, were significantly increased in diseased sheep compared with controls. Postmortem examination of dead or slaughtered animals showed enlarged icteric liver and have a marked lobular pattern with yellow white patches of necrotic lesions, However some cases show atrophied and marked fibrosed liver, in addition, histopathological examination of skin raveled hyperkeratosis, parakeratosis, acanthosis with vacuolated keratinocytes and infiltration of mononuclear inflammatory cells mainly lymphocytes,

moreover keratinized epidermis of the skin indicated severe parakeratosis with thick keratin deposition and infiltration of lymphocytes, however liver of dead or slaughtered animals show severe fibrosis of portal region with presence of edematous fluid around bile duct and portal vasculatures were found congested, furthermore, stenosis of bile duct due to hepatic fibrosis was detected with edematous fluids around portal region included bile duct .It had been concluded that the results revealed that the facial eczema syndrome was hepatogenic, light allergic eczema caused by toxic hepatic dysfunctions and hepatonecrosis in grazing sheep in this area.

INTRODUCTION

Facial eczema or Pithomycotoxicosis is a disease of domesticated animals including sheep, cattle and farmed deer's of all ages, although it can affect other grazing animals (1) Facial eczema may be defined as an acute obliterative cholangitis to which all other changes are secondary (2), It had a significant impacts on animals productivity, health and welfare and is considered as a common seasonal problem in farm animals (3).

The condition is caused by ingestion of spores of the fungus *Pithomyces chartarum,* which lives mainly on ryegrasses, however, under favorable conditions the fungus can rapidly multiply in pastures (4). The spores of the fungus release a potent mycotoxin known as sporidesmin in the gastrointestinal tract, which causes damage to the liver, bladder and mammary glands(5). The sporidesmins are excreted through the biliary system, in which they produce severe cholangitis and pericholangitis as a result of tissue necrosis, in addition biliary obstruction may also indicated, which restricts excretion of bile pigments and results in jaundice, similarly, failure to excrete phylloerythrin in bile leads to photosensitization(6).

Facial eczema is named for the visible signs of photosensitisation that affect non-pigmented areas of skin exposed to sunlight and result in severe skin irritation, dermatitis and fly strike like lesions, however, in some outbreaks of the disease, animals might show little or no visible skin lesions, but have suffered liver damage, therefore the disease considered as not well named or misnomer (7).The toxic liver injury commonly results in photodynamic dermatitis, since in sheep, the face is mostly the only site of the body that is readily exposed to ultraviolet light(8).In live animals, high levels of hepatic enzymes may reflect the extensive injury to the liver

(9).Production losses in dairy cattle and ewes arise from animal deaths, weight losses or reduced weight gain, reduced milk yield and reproductive performance are more findings common in this disease (10).In Basrah governorate little information's had been documented concerning Facial Eczema syndrome in sheep, therefore the present work were applied to study the clinical, hematological, biochemical and histopathological characteristic properties of this disease.

MATERIALS AND METHODS

Study design

The study was carried out on 523 local sheep breeds of different ages and of both sexes represents different herds, reared naturally in different areas of Basrah governorate. Fifty four(54) local sheep breeds were show different clinical sings including sings of photosensitization, parakeratosis, alopecia specially of face, intense itching, swelling of ears, anorexia and decreased milk production in milking ewes and twenty three (23) clinically healthy local sheep breeds were considered as controls. The study were documented at late summer and early autumn time /2015. Complete clinical examinations had been applied to all animals, moreover laboratory examinations for detection of endo and/or ecto parasitic loud using usual laboratory methods were also applied.

Blood collections and hematology

Ten milliliter (10ml) of blood were collected from each animal by jugular vein drainage, (2.5) milliliter of blood mixed with EDTA were used to determine Total erythrocyte count (TRBc), Hemoglobin concentration (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC) and total leukocytes count, (Hematology analyzer, Genex, USA), furthermore differential leukocytes count were done using Giemsa stain smears method according to Weiss and Wardrop (11). The remaining were used to obtained serum for evaluation of Zinc, Alanine aminotrasferase (ALT),Aspartate aminotrasfese (AST), Alkaline phosphatase (ALP),Total protein , Total bilirubin , Indirec and indirect bilirubin and Gamma glutamyltransferas (GGT), using available kids from (Egyption company for biotechnology.S.A.E /Egypt).

Gross post mortem examination and Histopathology

Some recently dead and /or slaughtered animals were examined for post mortem examination and laboratory histopathological evaluations after owner's approval. Skin specimens were collected from the alopecic patches of skin and liver, fixed in 10% neutral buffered formalin solution for 48 hrs, trimmed to apposite and suitable size, washed then dehydrated and cleared in xylol, embedded in paraffin wax, after that it were sectioned at 4-5 µ thickness, stained with hematoxyline and eosin, then examined under a light microscope (12).

Statistical analysis were done and the significance of variations between infected and healthy animals were evaluated through (SPSS) student t-test (13).

RESULTS

Diseased animals show signs of anorexia, salivation ,decrease milk production in milking animals , Transient diarrhea ,Hypotricosis specially of face with irregular patches of wool looseness, Fig (1), intense itching of different body parts Fig(2),Signs of parakeratosis, Fig (3), Since different area of skin become thickened, wrinkling with dandruff, swelling and dropping of ears ,Icteric mucous membranes specially of eyes ,Furthermore on clinical examinations diseased animals show rapid abdominal respiration ,tachycardia with strong heart beats , decrease ruminal contractions in active ruminant animals and increase body temperature (Table 1.and 2) .

Fig 1: Hypotricosis specially of face with irregular patches of wool looseness

Fig 2: Intense itching of different body parts

Fig 3: Signs of Hyperkeratosis and parakeratosis

Table 1: Clinical signs of diseased sheep with Facial eczema syndrome

Clinical signs	Diseased sheep n=54	%
Anorexia	49	90
Salivation	12	22.22
Decrease milk production in milking animals	34	63
Transient diarrhea	22	40.7
Hypotricosis specially of face	45	83.33
Intense itching of different body parts	41	76
Signs of parakeratosis	39	72.2
Swelling and dropping of ears	35	64.8
Icteric mucous membranes	29	53.7

On clinical examinations statistically significant increase ($p<0.05$) were encountered in body temperature, respiratory and heart rates, However ruminal contractions was decreased significantly (Table 2).

Table 2: Body temperature, respiratory and heart rate, and ruminal contractions of diseased sheep and controls.

Parameters	Controls n=23	Diseased sheep n=54
Body temperature C °	39.12 ± 1.21	41.3 ±1.2 **
Respiratory rate/ mint	21.88 ±6.73	80.2 ±10.6 **
Heart rate/ mint	87.3 ±8.4	120.2 ±13.56**
Ruminal contractions / 5 mints	3.42± 1.22	1.28± 1.65**

Values are mean ± standard error of mean. ** (P<0.05).

Results of hematological examinations show significant decrease in total RBC , Hb and PCV count reflecting Macrocytic hypochromic anemia ,Moreover total leukocytes count were also increased significantly due to increase lymphocytes and Eosinophiles.(Table 3).

Table 3: Blood parameters of diseased sheep and controls

Parameters	Controls n=23	Diseased sheep n=54
RBC $\times 10^6$	7.55± 1.23	4.83 ± 1.77 **
Hb g/dl	12.71 ± 2.66	7.39 ± 1.46 **
PCV %	32.53 ± 4.53	24.34 ± 4.67 **
MCV /fl	40.41 ± 4.55	52.39± 3.44 **
MCHC/dl	40.51 ± 7.77	29.43 ± 6.22 **
TLC $\times 10^3$	9.76 ± 3.25	13.22 ± 4.54 **
Lymphocytes (Absolute)	4352 ± 321.53	7364 ± 553.34 **
Nutrophiles (Absolute)	4284 ± 162.21	4225.46 ± 593.13
Monocytes (Absolute)	542 ± 62	513 ± 219
Eosinophiles (Absolute)	452 ± 134	988 ± 147**
Basophiles (Absolute)	83 ± 65	87 ± 73

Values are mean ± standard error of mean. ** (P<0.05).

Data concerning biochemical analysis revealed significantly decrease in total protein values and zinc, whereas ALT.AST.ALP. Total direct, indirect bilirubine and GGT , were significantly increased in diseased sheep compared with controls (Table 4).

Table 4: Biochemical parameters of diseased sheep and controls.

Parameters	Controls n=23	Diseased sheep n=54
Total protein (*g/dl)*	7.4± 1.23	5.3± 1.76**
ALT (*U/L)*	11.21± 2.34	22.51± 4.62
AST (*U/L)*	123± 11	228± 55**
ALP (*U/L)*	223±22	312±42**
Total bilirubine (*mg/dl)*	0.42±0.11	1.2± 0.24**
Direct bilirubine (*mg/dl)*	0.24± 0.11	0.9±0.12**
Indirect bilirubine (*mg/dl)*	0.18± 0.13	0.32± 0.11**
GGT (*U/L)*	77± 6.44	256.23± 7.32**
Zinc (*µg/ml)*	76.56 ± 3.8	33.25± 5.48**

Values are mean ± standard error of mean. ** (P<0.05).

Postmortem examination of dead or slaughtered animals showed enlarged, icteric, liver and have a marked lobular pattern with yellow white patches of necrotic lesions, however in some cases show atrophied and marked fibrosed liver, In addition, histopathological examination of skin raveled hyperkeratosis, parakeratosis, acanthosis with vacuolated keratinocytes and infiltration of mononuclear inflammatory cells mainly lymphocytes.Fig (4), Moreover keratinized epidermis of the skin indicated severe parakeratosis with thick keratin deposition and infiltration of lymphocytes. Fig (5). However livers of dead or slaughtered animals show severe fibrosis of portal region with presence of edematous fluid around bile duct and portal vasculature were found congested. Fig (6).Furthermore, stenosis of bile duct due to hepatic fibrosis was detected with edematous fluids around portal region included bile duct .Fig (7).Moreover other organs dose not show any gross or histopathological changes .

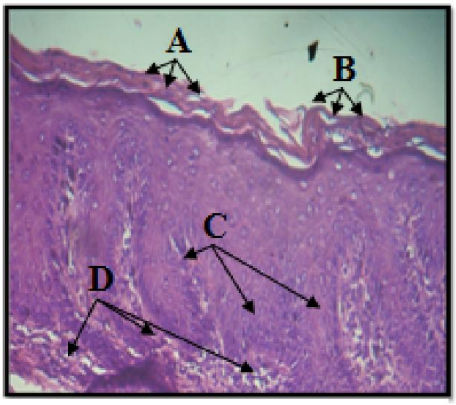

Fig 4: Histopathology of skin of diseased sheep with facial eczema syndrome showed A. Hyperkeratosis B. Parakeratosis C. Acanthosis with vacuolated keratinocytes. D. Infiltration of mononuclear inflammatory cells mainly lymphocytes. H&E stain. 10X.

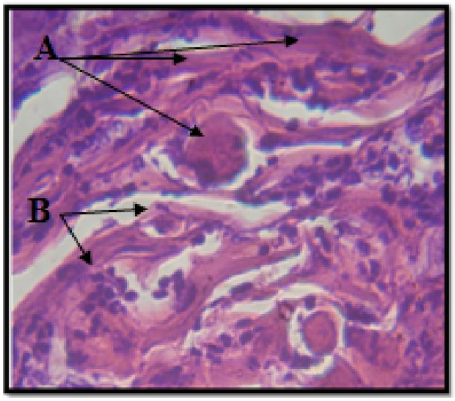

Fig 5: Histopathology of keratinized epidermis of skin of diseased sheep with facial eczema syndrome showed severe degree of parakeratosis A. thick keratin deposition B. Infiltration of mononuclear inflammatory cells (lymphocytes). H&E stain. 40X.

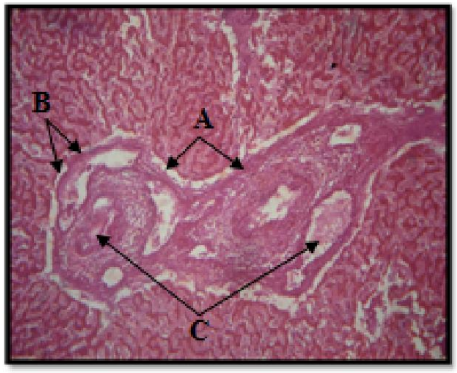

Fig 6: Histopathology of liver of dead sheep with facial eczema syndrome showed A. severe fibrosis of portal region B. edematous fluids around bile duct C. congested portal vasculatures. H&E stain. 10X.

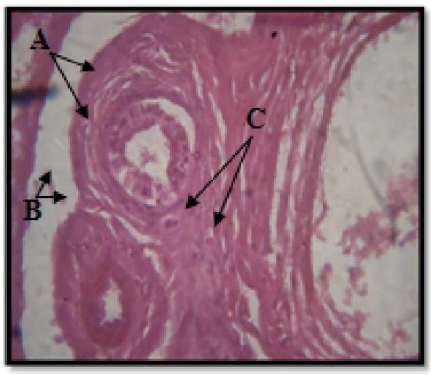

Fig 7: Histopathology of liver of dead sheep with facial eczema syndrome showed A. severe fibrosis of portal region and around bile duct caused stenosis. B. edematous fluids around portal region included bile duct. C. inflammatory cells H&E stain. 40X.

DISCUSSION

Facial eczema syndrome were suspected and recognized in Basrah governorate for the first time ,Since there were no any scientific documents clarify and mention this disease syndrome. In this mycotoxic disease of grazing livestock, the toxic liver injury commonly results in photodynamic dermatitis (14).

Facial eczema can have significant impacts on animal's productivity, health and welfare. Although the name suggests it is a skin disease, in most outbreaks most animals in a herd show little or may be less visible skin lesions, but have suffered liver damage. It is these animals that give the major economic impact (15).

Pastures tend to become toxic in late summer and autumn when periods of rain or high humidity occur in combination with high night-time minimum temperatures, However, to accurately predict Facial Eczema dangerous periods and take action to prevent liver damage before it occurs, use of a pasture spore monitoring program is essential (16).

Certain weather conditions are favorable to germination or sporulation, while ryegrass pastures can provide adequate substrate for fungal germination all year round (a low inoculum of *P. chartarum* spores over winter in Facial Eczema prone areas), the greatest development of the funguses from mid-summer with the death of the pasture. Late haymaking, topping or mowing of pastures may increase the substrate for fungal growth and sporulation, increasing pasture toxicity potential, The extent of defoliation during grazing largely determines intake of dead litter and spores very close grazing will increase the uptake of spores(17).

In the current study diseased sheep show different clinical manifestations which were in sporting data mention also by others (1,4,10), Mostly reflecting the photodynamic dermatitis and hepatic injury, Since The clinical manifestations were characterized by inflammatory edema in face (ears and eyelids) and even mandibular area. (Hepatic photosensititsation)(3,6,8).

Sporidesmin is released from ingested spores in the upper digestive tract, absorbed into the portal bloodstream and taken to the liver where it generates oxygen free radicals which damage cell membranes(5 and 18), Furthermore concentration of sporidesmin in the bile ducts lead to severe necrosis of their mucosal surfaces, resulting in rapid reduction of biliary secretion, bile duct thickening and eventual blockage, Cholangiohepatitis, ductular hyperplasia and fibrosis are also seen histologically(16).The resulting pericholangitis leads to obstructive jaundice, which reflected by the increase values of bilirubine (Total ,direct and indirect) in serum indicated in this study.

It had been documented that Phylloerythrin, a normal breakdown product of chlorophyll in the rumen, is normally absorbed into the portal bloodstream and

excreted by the liver in the bile, With the bile ducts blocked, it accumulates and spills over into the bloodstream, The reaction between circulating phylloerythrin and sunlight results in tissue damage (photosensitisation), and this is most severe in lightly colored and non-pigmented skin such as on the face, ears, lips, vulva and udders (15and 19).

Because of hepatic injury due to the disease condition specific biochemical changes were indicated such as total protein and specific enzymes were also altered in there activity, Therefore results of the present work raveled significant difference of most of them, As well, blood serum concentrations of the enzyme gamma glutamyl transferase (GGT) give the best indication of the severity of liver damage, or more specifically, bile duct damage. Although GGT is synthesised by many tissues, blood serum GGT originates mainly from the liver. Blood serum GGT activity principally increases in cholestatic disease.

Facial eczema causes much higher GGT levels as indicated in this study (20). Serum GGT concentrations may become elevated 2-3 weeks after exposure to sporidesmin ,Since the increase in serum GGT activity is proportional to the degree of hepatobiliary damage, Moreover GGT levels drop gradually over a period of several weeks after exposure to the toxin ceases, but often remain elevated for several months (2 and 17).

Furthermore Zinc had a protective role for Facial Eczema , as it forms a complex with sporidesmin, inhibiting its ability to cause cell damage, Since Facial Eczema prevention using zinc can be effective if it maintains the animals blood serum zinc level, Therefore feeding zinc oxide for example in grain/concentrates (in mash or pelleted form) in the bail at milking can be very effective for prevention of disease syndrome, However, the amount of zinc oxide included in each tone of grain concentrate for prevention dosing must be carefully calculated to achieve, It were indicated that diseased sheep in the current study were zinc deficient animals as the required zinc/kg of live weight/day were minimize the risk of zinc deficiency whereby decrease the prevalence of toxicity (21).

Results of gross examination of dead or slaughtered carcasses were agreed with (3 and 10) whom mentioned that severe icterus, hepatomegaly, enlarged gallbladder, congestion of mesenteric vessels were the common necropsy findings. Histopathological changes of the liver included necrosis of the hepatocytes,

cholangiohepatitis characterized by mononuclear inflammatory cell infiltrate in the portal area and mild to severe fibrosis around bile ducts. (2 and 9).

دراسة سريريه ومختبريه لمتلازمة اكزيما الوجه في ضأن محافظة البصرة

*كمال الدين مهلهل السعد ،*حسنين هشام ناصر العطيش و**جهاد عبدالامير احمد

*فرع الطب الباطني والوقائي **فرع الأمراض وأمراض الدواجن

كلية الطب البيطري / جامعة البصرة

الخلاصة

تم في هذه الدراسة فحص 523 من الضأن المحلية بأعمار مختلفة ومن كلا الجنسين، مثلت عدد من قطعان الأغنام والتي ترعى بصورة طبيعية في محافظة البصرة .أظهرت أربع وخمسون منها علامات سريرية تمثلت بالتحسس الضوئي ،نظير التقرن ،الصلع،الحك الشديد،تورم الأذنين،فقدان الشهية،وتناقص إنتاج الحليب في حين عدت ثلاث وعشرون منها سليمة سريريا مجموعة سيطرة ،تم اجراء الدراسة في صيف وخريف عام 2015.أجريت جميع الفحوصات السريرية اللازمة لكافة حيوانات الدراسة كما فحصت مختبرياً للتأكد من خلوها من إصابات الطفيليات الداخلية والخارجية . تبين من نتائج الدراسة إن الأغنام المصابة بالمرض عانت من فقدان الشهية التام ، سيلان اللعاب ، تناقص إنتاج الحليب في النعاج الحلوب، اسهال، تساقط الصوف وبخاصة من الوجه مكونة بقع جلدية غير منتظمة ،الحك الشديد في مناطق الجسم المختلفة،علامات نظيرالتقرن، تورم وتدلي الأذنين، اصفرار الأغشية المخاطية وبخاصة المبطنة للعين وعند فحص الحيوانات سريريا لوحظ تسارع التنفس ألبطني،ارتفاع معدلات ضربات القلب وقوتها ،تناقص تقلصات الكرش مع ارتفاع معدلات درجات حرارة الجسم فضلا عن ذلك فقد أظهرت الفحوصات الدموية تناقص معنوي في معدلات العدد الكلي لكريات الدم الحمر ،تركيزخضاب الدم ومعدلات كريات الدم الحمر المرصوصة سبب فقر الدم من النوع ذي الكريات كبيرة الحجم قليلة الصباغ ،كما ازداد معنوياً العدد الكلي لخلايا الدم البيض بسبب الزيادة المعنوية لأعداد الخلايا اللمفية والحمضات، كما بينت نتائج الدراسة حدوث تناقص معنوي في معدلات البروتين الكلي والزنك في حين ازدادت معنوياً معدلات خمائر ALT,AST,ALP والصفراوين الكلي والمباشر وغير المباشر ومعدلات خميرة GGT بالمقارنة مع مجموعة السيطرة كما اظهر التشريح المرضي للحيوانات المذبوحة أو النافقة تورم واصفرار الكبد وظهوره بمظهر تفصصي ملحوظ مع احتواءه على بقع نخرية بيضاء اللون في حين ظهرت اكباد لحيوانات اخرى بشكل ضامر متليف.كما تمثل الإمراض النسجي بظهور فرط التقرن، نظير التقرن، الشواك مع ملاحظة تفجي الخلايا المتقرنة وارتشاح للخلايا الالتهابية وبخاصة اللمفية فضلا عن ذلك لوحظت الطبقة المتقرنة لادمة الجلد موشحة بالتقرن الشديد مع رواسب كيراتينية ثخينة وارتشاح الخلايا اللمفية اما في كبد الحيوانات النافقة او المذبوحة جراء الاصابة فقد لوحظ تليف الجزء البابي مع تواجد الوذمة حول قناة الصفراء واحتقان الاوعية البابيه وبالاظافة إلى ذلك تم الكشف عن وجود تضيق القناة البابيه بسبب التليف الكبدي مع ارتشاح الوذمة حول المنطقة البابيه وبضمنها قناة الصفراء . استنتج من هذه الدراسة ان متلازمة اكزيما الوجة في الضأن هو مرض

كبدي المنشأ مع اكزيما تحسسية خفيفة تسببت بوساطة اختلال الوظائف السمي مع نخر كبدي للأغنام التي ترعى في هذة المنطقة.

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