Comunicación breve

HEPATIC LIPIDOSIS ASSOCIATED WITH MALNUTRITION AND PREGNANCY IN TWO BITCHES

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Abstract: *In some Latin American countries ascites has been observed to occur at different times after whelping in bitches fed low protein diets. The aim of this article was to describe two cases of bitches in which ascitis associated to hepatic lipidosis developed after parturition. Blood samples evidenced abnormalities compatible with liver disease. Abdominal paracentesis revealed an aseptic transudate fluid and ultrasonography hepatic hyperechogenicity. Definitive diagnosis was carried out by liver percutaneous needle ultrasound guided aspiration core biopsy. Histological findings showed dispersed parenchyma with macro and microvesicular fatty hepatocytes, some focus of intracellular cholestasis and isolated intralobulillar necrosis. Decreasing physical activity, a combination of furosemide and spironolactone and antibiotics for 21 days were indicated in both cases. Feeding modifications consisted on a high quality protein and low sodium diet. Ascitis decreased within the 3 days of treatment in both cases. Six weeks after the first consultation one bitch remained in a good clinical condition while the other one died. It is concluded that, in bitches, hepatic lipidosis can be considered as a post partum problem when the anamnesis reveals a long term hypoprotein diet.*

Key Words: lipidosis- malnutrition- pregnancy- bitch

LIPIDOSIS HEPÁTICA ASOCIADA CON MALNUTRICIÓN Y PREÑEZ EN DOS PERRAS

Resumen: *En algunos países latinoamericanos se observó que la ascites ocurre en diferentes momentos post parto en perras alimentadas con dietas hipoproteicas. El objetivo de este articulo fue describir 2 casos de perras con ascitis asociada a lipidosis hepática desarrollada después del parto. Las muestras de sangre evidenciaron anormarmalidades compatibles con enfermedad hepática. La paracentesis abdominal reveló un trasudado aséptico y la ultrasonografía hiperecogenicidad hepática. Se arribó al diagnostico definitivo por biopsia por aspiración con aguja percutanea ecodirigida del hígado. Los hallazgos histológicos muestraron un parénquima disperso con hepatocitos con grasa macro y microvesicular, algunos focos de colestasis intracelular y necrosis aislada intralobulillar. En ambos casos se indicó reducir la actividad física, una combinación de furosemida y espironolactona y antibioticos por 21 días. Las modificaciones en la alimentación consistieron en administrar una dieta con proteínas de alta calidad y baja en sodio. La ascitis decreció dentro de los 3 días de tratamiento en ambos casos. Seis semanas después de la primera consulta una de las perras mejoró su estado clínico y la otra murió. Se concluye que, en perras, la lipidosis hepática puede ser considerada como un problema post parto cuando la anamnesis revela una dieta prolongada hipoproteica.*

Palabras claves: lipidosis- malnutrición- preñez- perra

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INTRODUCTION

Hepatic lipidosis is defined as the excessive storage of fat in the liver cells. It is an acquired liver disease that has been related to multiple etiologies such as starvation, diabetes mellitus, obesity, drug injury and toxicities in both dogs and cats (1).

In humans hepatic lipidosis has been associated, among other causes, either with malnourishment or pregnancy (2,3). The Kwashiorkor disease is a protein deficiency syndrome described in young children fed with a carbohydrate diet. It is characterized by generalized edema, apathy and a macrovesicular fatty hepatopathy (3). These hepatic changes are known to be due to both fat movement from body deposits and to lipoprotein synthesis disorders (3).

In late pregnant women, it has been described an uncommon severe liver disease which histologic hallmark is microvesicular fatty hepatic changes usually associated with inflammatory cell infiltrates within the lobules as well as canalicular cholestasis. Although the exact etiology of this hepatic condition has not been yet well understood, it is suggested that mitochondrial injury might be involved in its pathogenetic pathway (2, 4, 5). There may, very probably, be subclinical milder forms of this last hepathopaty (2, 4).

During the last years, in some Latin American countries, ascites has been observed to occur at different times after whelping in bitches fed low protein diets (unpublished observation). Up to our knowledge, these bitches were never studied in detail. The aim of this article was to describe two cases of bitches in which ascitis associated to hepatic lipidosis developed after parturition. Due to the similarity of both cases they were described together throughout the article and differences pointed out.

CASE REPORTS

A 4 year old Pekinese and a 3 year old Siberian Husky bitches with ascitis were referred to La Plata Veterinary Faculty during 2002. Both bitches were multiparous, had whelped normally their last litters 6 months ago and had no history of drugs administration. Their litters were of 5 and 9 puppies, respectively, they were all normal at birth, although the ones of the Pekinese bitch died within their first month of life because of unknown reasons.

For nearly a year before consultation the bitches had been fed a low protein diet, based mainly on carbohydrates (90% rice or pasta). According to history, in both cases abdominal distension was first noticed one month after parturition and then gradually increased. The bitches were in a poor body condition, slightly depressed and weak with pale mucus membranes at the moment of the first consultation. Their abdomen were distended and tense evidencing fluid content (Figures 1 a, b). Their appetite was conserved and body temperature normal in the Siberian bitch, although rectal temperature was 39 ºC in the Pekinese bitch.

Diagnosis

The eventual association of ascitis to heart failure was ruled out by a complete cardiologic examination based on ECG and echocardiog-raphy. Blood samples were taken for hemogram and biochemical profile. Results are shown in Table 1. Urianalysis revealed normal findings in both cases. Abdominal ultrasonography showed hypoechoic fluid compatible with ascitis and a normal sized hyperechoic liver with mild signs of portal hypertension (6; Figure 2). Abdominal paracentesis was carried out for cytological, biochemical and microbiological analysis. Results revealed the aseptic transudate characteristics of the ascitis fluid in both cases (Table 2).

Definitive diagnosis was carried out by liver percutaneous needle ultrasound guided aspiration core biopsy. Tissue samples obtained were fixed in 10 % formalin, embedded in paraffin and stained with hematoxylin and eosin according to routine procedures for histological study (5). Histological findings evidenced dispersed parenchyma with macro and microvesicular fatty hepatocytes, some focus of intracellular cholestasis and isolated intralobulillar necrosis (Figure 3).

Treatment

No specific therapy has been described for hepatic lipidosis (2, 8). Decreasing physical activity and a symptomatic - supportive therapy were indicated in both cases (2, 8, 9). A combination of furosemide 3 mg/kg q 8 h IM and spironolactone 3 mg/kg q 24 h PO was administered during the first 21 days. Amoxicillin 22 mg/kg PO q 12 h for 21 days was also indicated in both cases. Feeding modifications consisted on the indication of a home made highly digestive, high quality protein and low sodium diet (8, 10).

Follow Up

In both bitches general condition improved gradually within the 3 days of treatment and ascitis were mild at that moment.

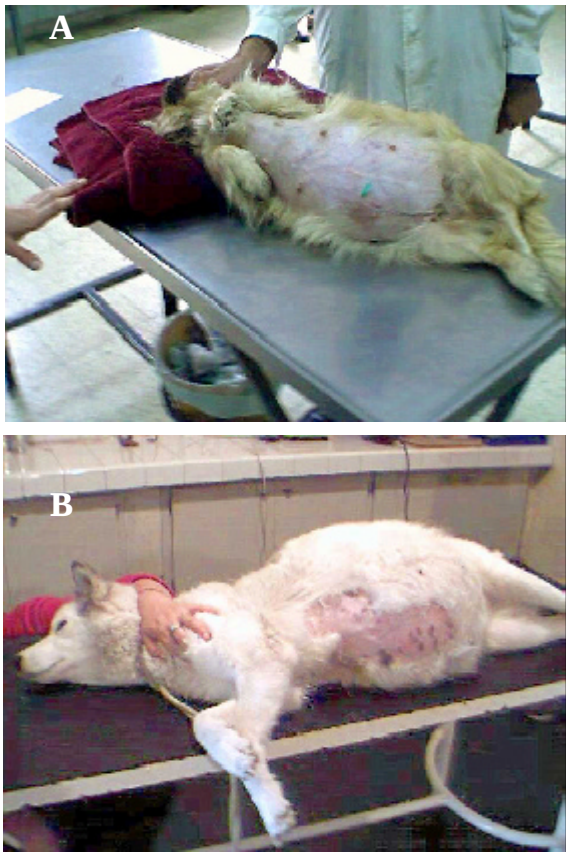

Figure 1. a) Pekinese bitch. b) Siberian Husky bitch. Both pictures were taken on the day of the first presentation. A marked abdominal distension could be seen.

Figura 1. a) Perra Pequines b) Perra Siberiana Husky. Ambas fotos se tomaron en el día de la primera visita. Se observa una marcada distensión abdominal

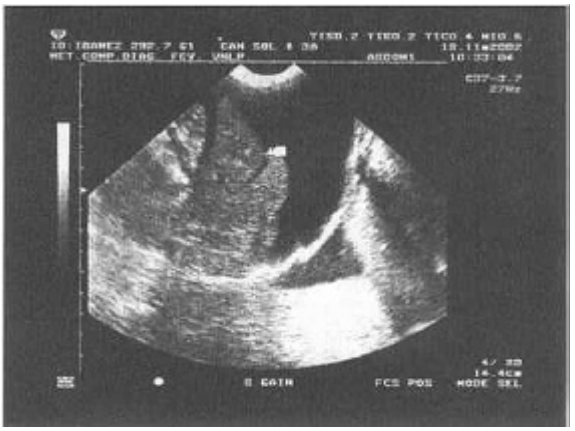

Figure 2. Abdominal ultrasonography. Hypoechoic fluid compatible with ascitis (right) and a hyperechoic liver (left).

Figura 2. Ultrasonografía abdominal. Fluido hipoecoico compatible con ascitis (derecha) e hígado hiperecoico (izquierda).

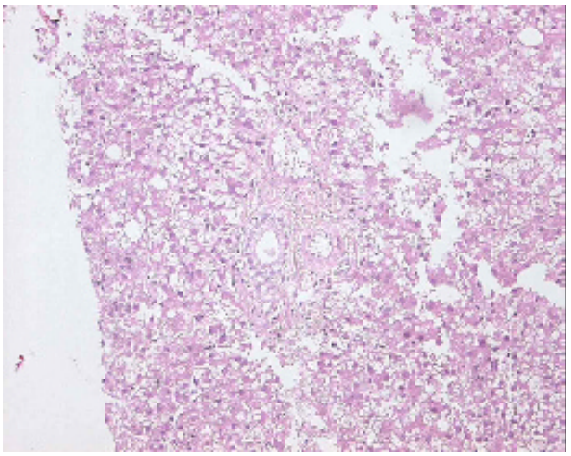

Figure 3. Liver histology showing microvesicular fatty change of hepatocytes. Notice that some large lipid droplets distending the hepatocyte cytoplasms were also present. (H&E x 80).

Figura 3. Histología hepática mostrando cambios grasos microvesiculares de los hepatocitos. Nótese que también están presentes algunas gotas grandes de lípidos que distienden los citoplasmas de los hepatocitos (H&E x 80).

One week later, the animals had gained weight and ascitis was absent. A second hepatic aspiration was not permitted by the owners. The Siberian bitch remained in good physical condition at the time of her last visit to the Faculty 6 weeks later the first consultation, while the Pekinese died on the same week. Unfortunately, necropsy was not allowed by the owner.

DISCUSSION

Hepatic lipidosis is a potentially reversible condition if the primary problem is controlled (1). Most human patients with macrovesicular fatty liver changes are asymptomatic and have modest biochemical test abnormalities (4, 10). Conversely, microvesicular fatty change is a more ominous finding than its large droplet counterpart. Although, in pregnant women who survive, the fat rapidly remits, disappearing in a few weeks and normal hepatic histology is restored (4).

In the present cases, hemogram (anemia in both bitches, and mild leukocytosis and lymphopenia in the Pekinese bitch indicating an stress response) and serum (decreased urea in the Pekinese, increased alkaline phosphatase in the Siberian and a decreased albumin/globulin ratio in both bitches) parameters revealed abnormalities compatible with liver disease, being more severe in the Pekinese bitch (10, 11). Ascitis could be attributed to both hypoalbuminemia and portal hypertension. The histologic liver findings evidenced

Table 1: Hematology and chemistry profiles of the bitches suffering post partum ascitis.
Tabla 1: Hematología y perfiles químicos de las perras con ascitis post parto.

	Pekinese bitch	Siberian Husky bitch
Erithrocytes mm^3	4.210.000	3.000.000
Packed cell volume (%)	27.4	22
Hemoglobin g%	8.9	7.5
Leukocytes mm^3	19.600	11.000
Mature neutrophils (%)	91	65
Band neutrophils (%)	0	2
Eosinophils (%)	1	8
Lymphocytes (%)	8	25
Basophils (%)	0	0
Monocytes (%)	0	0
Glucose (mg/dl)	68	94
Urea (mg/dl)	11	35
Creatinine (mg/dl)	0.44	1.05
Total Cholesterol (mg/dl)	77	149
Total protein (g/dl)	4.9	6.7
Albumin (g/dl)	2.1	2.4
Globulin (g/dl)	2.76	3.79
Albumin/ Globulin	0.78	0.69
Total bilirubin (mg%)	0.18	0.45
Alkaline phoshatase (U/L)	124	310
AST (SGOT) (U/L)	117	22
ALT (SGTP) (U/L)	60	17

Table 2: Analysis of ascitis fluid of the same animals.
Tabla 2: Análisis del liquido ascítico de las mismas perras.

	Pekinese bitch	Siberian Husky bitch
Aspect	watery	watery
Density	1.010	1.010
Total protein g/dl	100	50
Rivalta reaction	positive	negative
Glucose mg/dl	100	60
Bilirubin	negative	negative
pH	8	7.5
Bacteriological exam	negative	negative
Bacteriological culture	negative	negative
Cytological exam /mm3	100	100

mixed macro and microvesicular fatty changes, characteristic of both Kwashiorkor and pregnancy fatty liver in humans, respectively. In spite of the fact that a second hepatic aspiration was not carried out, the complete clinical recovery within 6 weeks might suggest the reversibility of the liver changes in the Siberian Husky bitch.

Interestingly, late pregnancy lipidosis presentation in women appears in a period approximately equal to the 2 month canine pregnancy plus the six months that the condition took to become clinically evident in both animals. Hepatic changes in the Siberian and the Pekinese might be a mild and a severe form, respectively of the human pregnancy fatty liver.

Actually, the exact etiopathogenesis of the liver changes of these cases could not be fully explained in the present article. In humans, Kwashiorkor signs appear in young children, when protein requirements are essential. We hypothesized that a similar situation could be true in pregnant and lactating bitches triggering the syndrome.

If the hepatic changes in these bitches represented a combination of both human syndromes or if one of them was primary remains to be elucidated. Although, more animals with

this problem should be studied in detail, it is concluded that, in bitches, hepatic lipidosis can be considered as a post partum problem when the anamnesis reveals a long term hypoprotein diet.

REFERENCES

1. Johnson SE. Diseases of the liver. In: Ettinger SJ Feldman EC Textbook of Veterinary Internal Medicine 4th ed. Philadelphia, B.W. Saunders. 1995; 1313-1358.

2. Jeffries GH. Liver diseases. In: Beeson PB; Mc Dermott W (ed) Textbook of Medicine 14th ed. Philadelphia, B.W. Saunders. 1975; 1107-1207.

3. Scrimshaw S. Nutritional diseases. In: Beeson PB; Mc Dermott W (ed) Textbook of Medicine 14th ed. Philadelphia, B.W. Saunders. 1975; 842-924.

4. Lee RG. Fatty change and steatohepatitis. Diagnosis Liver Pathology Philadelphia, Mosby. 1994; 167- 194.

5. Snover DC. Nonneoplastic Liver Disease. In: Sternberg, SS. Diagnostic Surgical Pathology 3rd ed. Philadelphia, Lippincott Williams & Wilkins. 1999; 1509-1621.

6. Hunt CM, Sharara AI. Liver disease in pregnancy. Am Fam Physician. 1999; 15; 59 (4): 829-836.

7.Nyland TG, Matton SJ, Winer ER. Ultrasonography of the liver. In: Nyland, TG, Matton SJ. Veterinary ultrasound. Philadelphia, B.W. Saunders. 1995; 52-72,

8. Bunch SE. Specific and symptomatic medical management of diseases of the liver. In: Ettinger SJ Feldman EC Textbook of Veterinary Internal Medicine 4th ed. Philadelphia, B.W. Saunders. 1995; 1359-1371.

9. Everson GT. Liver problems in pregnancy: part 2. managing pre-existing and pregnancy-induced liver disease. Medscape Womens Health. 1998; 3 (2): 2

10- Ochs A. Acute hepatopathies in pregnancy: diagnosis and therapy. Schweiz Rundsch Med Prax 1992; 18; 81 (34): 980-982.

11. Center SA. Pathophysiology and laboratory diagnosis of liver disease. In: Ettinger SJ Textbook of Veterinary Internal Medicine 3rd ed. Philadelphia, B.W. Saunders. 1992: 1421-1478.