A CASE OF INTESTINAL LYMPHANGIECTASIA WITH LIPOGRANULOMATOUS LYMPHANGITIS IN A FEMALE ROTTWEILER DOG

UM CASO DE LINFANGIECTASIA COM LINFANGITE GRANULOMATOSA NUMA CADELA ROTTWEILER

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Abstract: *A three year old female Rottweiler dog was presented with clinical signs of chronic diarrhoea, severe weight loss and sporadic vomiting. Histopathology revealed intestinal lymphangiectasia with lipogranulomatous lymphangitis. Intestinal lymphangiectasia represents a pathological dilatation of the intestinal lymph vessels and is the most common cause of protein-losing enteropathy in the dog. This paper reports a clinical case with a short review of literature..*

Resumo: *Uma cadela, fêmea, de raça Rottweiller de três anos de idade apresentou-se com sinais clínicos de diarreira crónica, perda de peso grave e vómito esporádico. A histopatologia revelou uma linfangiectasia intestinal com linfangite lipogranulomatosa. A linfangiectasia intestinal consiste numa dilatação patológica dos vasos linfáticos intestinais, sendo a causa mais frequente de enteropatia com perda de proteína no cão. Este trabalho consiste na apresentação do caso clínico e numa breve revisão da literatura*

INTRODUCTION

Intestinal lymphangiectasia (IL) is an uncommon disease but an important cause of protein-losing enteropathy in the dog. The major morphological abnormality that characterizes this disease is marked dilation of intestinal lymphatic vessels in the mucosa, submucosa and serosa (Finco et al., 1973; Melzer & Sellon, 2002; Batt & Hall, 1989).

It has been recognized as a clinical entity in humans since 1961 and has been first described in dogs in 1968 (Waldmann, 1966; Campbell et al., 1968; Finco et al., 1973; Mattheeuws, 1974).

The clinical signs of IL can be quite variable. Many dogs with IL exhibit nonspecific signs, such as anorexia or lethargy. Diarrhoea is one of the most consistent clinical signs associated to this disease, although not seen in all patients (Griffiths et al., 1982; Melzer & Sellon, 2002). Effusions or oedema, more often pure transudates effusions, may develop when serum albumin concentrations fall below 1.5 g/dl (Melzer & Sellon, 2002).

Laboratory abnormalities can support the IL diagnosis; however they are neither specific nor pathognomonic of the disease (Kull et al., 2001).

CASE DESCRIPTION

A three year old female Rottweiler, 45 kg b.w. was admitted for consultation at the teaching hospital of the Veterinary University (FMV-ULHT) with a two months history of chronic diarrhoea, severe weight loss and sporadic vomiting. The owner described large amounts of brown watery stools, with no mucus or fresh blood, 3 to 4 times a day and no tenesmus.

The dog was eating well, was alert and responsive, although he had lost 13 kg in two months.

Previous exams performed by the referring vet revealed hypoproteinemia (3.2 g/dL,

reference range: 5.0 to 7.2 g/dL), lymphocytosis (5.7x109/L, reference range: 0.8 to 5.1x109/L) and thrombocytopaenia (84x109/L, reference range: 117 to 460x109/L). The diarrhoea did not respond to various antibiotic treatments or dietary management (hypoallergenic diet) and there was no complete improvement of symptoms.

On admission, clinical examination revealed mild abdominal discomfort, distended abdomen and emaciation.
Blood, biochemical profile, abdominal ultrasound and radiography were performed.

Hematological findings showed mild lymphocytosis (5.7x109/L, reference range:0.8 to 5.1x109/L) and thrombocytopaenia (84x109/L, reference range:117 to 460x109/L).
Biochemical profile showed moderate hypoproteinemia (4.2 g/dL, reference range: 5.0 to 7.2 g/dL) with hypoalbuminemia (1.7 g/dL, reference range: 2.3 to 4.0 g/dL). Cholesterol level was border line, 112 mg/dL (reference range: 110 to 321 mg/dL). Liver was apparently normal with alanine aminotransferase of 50 u/l (reference range: 47 to 254 u/l).
Urinalysis was within normal limits.
Radiographic exam was unremarkable except for a slight splenomegaly (figure 1).

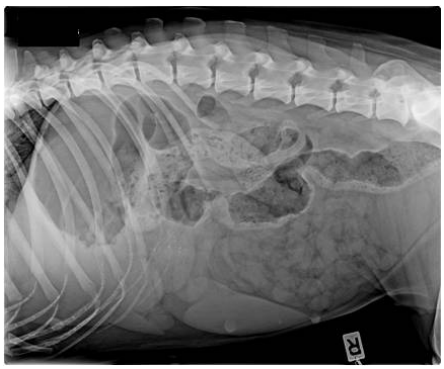

Figure 1 – Lateral abdominal radiograph showing slight splenomegaly

Abdominal ultrasound examination revealed an increase of the small intestinal wall (8 mm), with normal layering, mild hipermotility and preserved function. Some intestinal segments had dilated lumen with anechoic content. It was identifiedmild splenomegaly with normal echogenicity and architecture, without focal or diffuse abnormalities. The colon had some faecal content and the mesenteric lymphnodes were normal (figure 2).

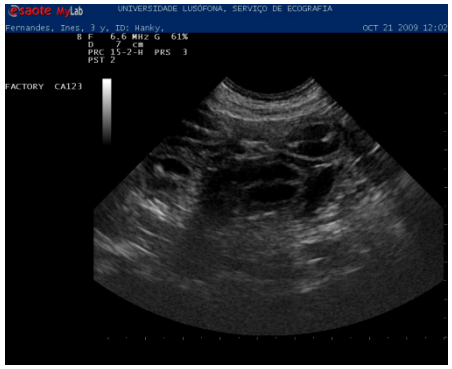

Figure 2 – Transverse ultrasonogram of some sections of small intestine illustrating increase of the wall with normal layering.

At that time, the animal was medicated with metronidazol at a dosage of 15mg/kg, twice daily (Flagyl®, Sanofi-Aventis) and amoxicilin potenciated with clavulanic acid at a dosage of 12,5mg/kg, twice daily (Synulox®, Pfizer). Pancreatic enzymes were prescribed at a dosage of one capsule twice daily, with meals (Kreon®, Solvayfarma) as well as an ultra-low-fat diet supplemented with peanut oil. Cimetidine at a dosage of 5mg/kg, twice a day (Tagamet®, Smith Kline & French) and Vitamin B12 at a dosage of 1000 µg/dog once a week, for six weeks, (OHB12 5000 µg, Jaba Recordati).
Clinical and imaging findings were compatible with the following differential diagnosis of protein-losing enteropathy (ex: intestinal lymphangiectasia) and severe chronic enteritis (ex: severe small intestinal IBD- inflammatory bowel disease –, with SIBO- small intestinal bacterial overgrowth, acute ulcerative enteritis and small intestinal neoplasia (ex: alimentary lymphoma).

An exploratory celiotomy was recommended in order to collect intestinal and stomach full thickness biopsies.
To minimize the anaesthetic risk and post operative complications, a plasma transfusion was done to increase short-term the albumin level.
During the surgery, the presence of multiple small white nodules along ectasic lymphatic vessels on the serosal surface of the small intestine was evident. Furthermore, prominent mesenteric lymph vessels were distended with thick and chalky white paste (figure 3). Liver surface was irregular with visible alterations and a liver guillotine type biopsy was performed.

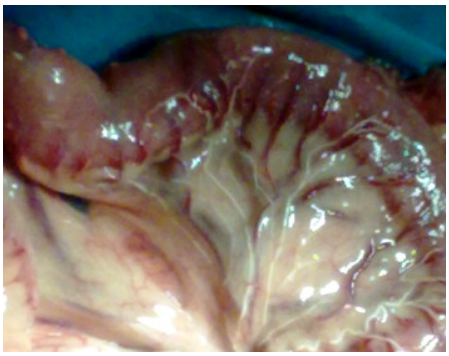

Figure 3 – Intraoperative image of distended and prominent mesenteric lymph vessels. Note the focal whitish points enlargements corresponding to lipogranulomas on the anti-mesenteric serosal surface.

Histopathological findings revealed a thicker intestinal mucosa due to lymphatic vessels ectasia and lymphoplasmacytic infiltrate in the lamina propria. The submucosa showed dilated lymphatic vessels, and in the subserosa, several lipogranulomes composed of foamy machrophages, were observed on the periphery of ruptured lymphatic vessels. The liver biopsy showed dilated lymphatic vessels in the periportal area, and mild hepatocyte vacuolar degeneration.
The histopathological diagnosis was intestinal lymphangiectasia with lipogranulomatous lymphangitis and hepatic-lymphatic congestion with vacuolar degeneration.

DISCUSSION

IL is an uncommon disease in the general canine population, but is one of the most common causes of gastrointestinal protein loss. Its inheritance is still unknown but breeds with a higher incidence of IL due to inflammatory diseases include Basenjis, Soft-coated Wheaten Terriers, and Lundehunds (Melzer & Sellon, 2002; Littman et al., 2000; Landsverk & Gamlem, 1984).
This disease can be primary or secondary and, in contrast to human IL, canine congenital IL is considered less common than acquired IL (Finco et al., 1973; Melzer & Sellon, 2002).
Acquired IL is mainly idiopathic, but can also be recognized most frequently due to inflammatory processes that block lymphatic vessels and lymph flow. Other causes of increased pressure in lymph vessels include portal hypertension resulting from cirrhosis or heart disease (i.e., right-sided heart failure, pericardial effusion and pericarditis). Although, less frequently, we can also see cases with associated tumours of the intestinal wall, mesentery or even metastatic tumours (Melzer & Sellon, 2002; Louvet & Denis, 2004).
Congenital IL, rarely reported, is caused by abnormally formed lymphatic vessels (Fogle & Bissett, 2007).
The diagnosis of IL in dogs can be challenging. Clinical signs of IL can be highly variable, as many dogs with IL exhibit nonspecific signs such as lethargy or anorexia; however, diarrhoea remains the most common clinical feature, especially small bowel diarrhoea (Fogle & Bissett, 2007).
Ascites, oedema, and hydrothorax are common in dogs with IL, mainly found due to decreased oncotic pressure secondary to hypoproteinemia, (especially hypoalbuminemia). In some dogs, clinical signs of thromboembolic disease, such as tachypnea and dyspnea due to pulmonary thromboembolism, may develop (Melzer & Sellon, 2002).

As previously described, laboratory findings in dogs with IL may suggest intestinal loss of lymph; however, they are not specific for a definitive diagnosis. Lymphopenia is the most frequent change supportive of IL, although in this case it was not observed. Anaemia and neutrophilic leukocytosis, (due to chronic inflammation) may be present in some dogs, however, not verified in this one. In this case, hypoalbuminemia was verified and this is the most consistent laboratory abnormality reported in canine IL. In some cases it can even be noticed pan-hypoproteinemia (Melzer & Sellon, 2002; Burns, 1982).

Hypocholesterolemia is another frequent biochemical alteration seen in canine IL although, was also absent in this case.

Other biochemical abnormalities reported include hypocalcemia secondary to overall loss of bound calcium resulting from hypoalbuminemia, and secondary to poor absorption as also vitamin D from the gut and by the lipogranuloma formation within the lymph vessels. Total serum calcium level is often decreased as an artefact of low serum albumin concentration (Melzer & Sellon, 2002; Burns, 1982; Fogle & Bissett, 2007; Mellanby et al., 2005).

Thrombocytopenia, although unusual in IL cases, was seen in this dog. Some authors suggest this finding as a complication of the disease, such as thromboembolism or disseminated intravascular coagulation, however, no signs of these diseases were observed (Melzer & Sellon, 2002).

The IL diagnosis is only confirmed by intestinal biopsy specimens (Kull et al., 2001).

In this case surgical biopsy samples were performed by laparotomy due to the advantages of obtaining full-thickness lymphatic architecture and less disruption of the normal structure when compared to samples collected by endoscopy (Fogle & Bissett, 2007).

The whitish spots observed in the small intestinal serosal surface and prominent dilated mesenteric lymph vessels corresponded to lipogranulomatous lymphangitis on histopathological examination. Not all cases of canine intestinal lymphangiectasia show this type of lesions and it is believed that this lipogranulomes result from an inflammatory foreign body type reaction. This inflammatory reaction is rich with macrophages that appear not only due to the extravasation of lipid content, through dilated wall or ruptured lymph vessels, but also secondary to stagnated chylous and fat in perilymphatic tissues (Langley-Hobbs, 1993).

Increased activities of liver enzyme and vacuolar changes in hepatocytes have been described in dogs with IL (Finco et al., 1973; Fogle & Bissett, 2007). In this case, although there were no changes in biochemical liver function, histological appearance of the liver was consistent with lymphatic congestion and vacuolar degeneration.

Urinalysis results are important as differential diagnosis for hypoalbuminemia secondary to renal protein lost (Melzer & Sellon, 2002). In this dog urinalysis results were unremarkable as in all IL cases.

The gold of therapy in secondary IL cases includes treatment of underlying disease. In primary lymphangiectasia cases, treatment is basically supportive and symptomatic. Affected patients should have dietary modification with specific nutritional treatment, including low-fat food and supplements with adequate amounts of essential fatty acids, a reduction in long-chain triglycerides, because they stimulate the loss of lymph to the gastrointestinal lumen by chylomicron formation.

Long-chain triglycerides are not advisable in IL affected animals. Although there is some controversy about the mechanism of absorption for medium-chain triglycerides (MCTs), it is felt that MCTs can provide some of the favourable aspects helpful in recovering the patient's body condition, without stimulating lymph loss (Peterson & Willard, 2003; Melzer & Sellon, 2002; Brooks, 2005).

To ensure the success of nutritional treatment is also really important to choose high-quality and highly-digestible protein sources, so that we can minimize protein indigestion and reduce the production of toxins by bacterial flora.
Immunosuppressive therapy with glucocorticoids may be useful in some specific cases, especially when the disease is secondary to an inflammatory cause. Prednisone at immunosuppressive doses (2 to 4 mg/kg/day) is commonly used in the initial management of many dogs with IL and mucosal inflammation. In patients that respond poorly to glucocorticoids or in severe cases, azathioprine may be added (1 to 2 mg/kg or 50 mg/m2 PO q24–48h). In this case no glucocorticoids were prescribed.
Antibiotherapy with metronidazole is also indicated not only because of its antimicrobial effectiveness, but also by their immuno-modulatory capabilities (Pibot et al., 2006; Hand & Novotny, 2002; Melzer & Sellon, 2002).
As demonstrated in this case, a favourable outcome could be achieved with specific dietary management and supportive therapy, without glucocorticoid therapy.
The main goal of treatment is the control of clinical signs, without cure. Previous studies reported a 2 years survival time after diagnosis (Hand & Novotny, 2002; Griffiths et al., 1982; Melzer & Sellon, 2002).

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