



Ultrasound and endoscopic findings in dogs with lymphangiectasia

[Conclusões ultrassonográfica e endoscópica em cães com linfangiectasia]

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ABSTRACT

Lymphangiectasia is a heterogenous inflammatory bowel disease characterized by lymphatic vessel dilation, chronic diarrhea and protein loss such as serum albumin and globulin. The most common cause of lymphangiectasia is considered to be the congenital malformation of the lymphatics. The study was conducted between 2012-2015 on 76 dogs suffering from intestinal disorders and manifesting digestive symptoms such as diarrhea or weight loss. In order to assess the origin of disorder, physical examination, biochemistry profile, ultrasound and endoscopic examinations were performed. Ultrasound examination tried to assess the changes of intestines' echogenicity, changes in wall thickness, wall layering and presence of striations or / and speckles (hyperechoic structures along intestinal mucosal layer). Endoscopic examination findings included dilated lacteals (59.2%) and erythema (21.1%). Although increased friability was observed in 33 dogs, it was not considered in the study due to limitations represented by the evaluation of the endoscopic images only. The study proved that an extremely significant statistical correlation exists between the presence of speckles and dilated lacteals in dogs with lymphangiectasia ($P < 0.05$). Up to now, there is no other study to make an association between the white spots observed in ultrasound examination and dilated lacteals revealed after endoscopy in dogs with intestinal lymphangiectasia.

Keywords: dogs, lymphangiectasia, ultrasound, endoscopy

RESUMO

A linfangiectasia é uma doença inflamatória intestinal heterogênea, caracterizada por dilatação dos vasos linfáticos, diarreia crônica e perda de proteínas, como albumina sérica e globulina. A causa mais comum de linfangiectasia é considerada a malformação congênita dos linfáticos. O presente estudo foi realizado entre 2012 e 2015, em 76 cães que sofrem de distúrbios intestinais e manifestam sintomas digestivos, como diarreia ou perda de peso. Para avaliar a origem do distúrbio, foram realizados exame físico, perfil bioquímico, ultrassonográfico e endoscópico. O exame ultrassonográfico tentou avaliar as alterações da ecogenicidade do intestino, as alterações na espessura da parede, a estratificação e a presença de estrias e / ou de manchas (estruturas hiperecoicas ao longo da camada mucosa intestinal). Os resultados do exame endoscópico incluíram lacteais dilatadas (59,2%) e eritema (21,1%). Embora tenha sido observada maior friabilidade em 33 cães, ela não foi considerada no estudo devido às limitações representadas pela avaliação apenas das imagens endoscópicas. O estudo demonstrou que existe uma correlação estatística extremamente significativa entre a presença de manchas e lacteais dilatadas em cães com linfangiectasia ($P < 0,05$). Até o momento, não há outro estudo para associar as manchas brancas observadas no exame ultrassonográfico e lacteais dilatadas reveladas após endoscopia em cães com linfangiectasia intestinal.

Palavras-chave: cães, linfangiectasia, ultrassom, endoscopia

INTRODUCTION

Intestinal lymphangiectasia is a heterogenous inflammatory bowel disease characterized as a protein-losing enteropathy. This disease has been reported as a prequel to hypomagnesemia and

secondary hypoparathyroidism with resultant lymphocytic-plasmacytic enteritis (Brooks, 2005; Rodriguez-Alarcon *et al.*, 2012). Clinically affected dogs are usually large-breed dogs where a higher incidence of gastric carcinoma and gastritis is associated with this disease (Brooks,

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2005; Rodriguez-Alarcon *et al.*, 2012). Lymphangiectasia is characterized by lymphatic vessel dilation, chronic diarrhea and protein loss such as serum albumin and globulin (Gaschen, 2013). The lymphatic vessels are vascular channels that transport lymph, a clear fluid that contains white-blood cells. This fluid circulates through the lymphatic vessels, removing bacteria and other materials from body tissues, also serving the transport of fats from the small intestines (Sutherland-Smith *et al.*, 2007). The most common cause of lymphangiectasia is considered to be the congenital malformation of the lymphatics.

Secondary lymphangiectasia may be caused by granulomas or neoplasia causing lymphatic obstruction, or increased central venous pressure causing abnormal lymph drainage (Penninck *et al.*, 2003). Inflammatory bowel disease can also lead to inflammation of the lymphatics and lymphangiectasia through migration of inflammatory cells through the lymphatics. Chronic diarrhea is almost always associated with lymphangiectasia, but most other signs are linked to low serum protein levels (hypoproteinemia), which causes low oncotic pressure (Gaschen, 2013). These signs include ascites, pleural effusion, and edema of the limbs and trunk. Weight loss is also observed in chronic evolution of lymphangiectasia.

Numerous studies tried to assess the changes that occur at the level of digestive tract in dog patients with digestive disorders, either by ultrasound or endoscopic examination but few have provided in depth analysis regarding the changes that are observable both in ultrasound and endoscopic investigations (Melzer and Sellon, 2002, Malancus, 2015). The present study tried to assess the specific changes observed in dogs with lymphangiectasia and correlate the ultrasound and endoscopic results. The starting hypothesis of the study stated that there are no significant correlations between the ultrasound and endoscopic aspects in patients with lymphangiectasia.

The research tried to assess all the changes that can be noticed under ultrasound and endoscopic examination. Up to now, this is the first study to make an association between the white spots observed in ultrasound examination (speckles)

and dilated lacteals revealed after endoscopy in dogs with intestinal lymphangiectasia.

MATERIAL AND METHODS

The study was undertaken in a private veterinary clinic from Dorset area, UK, between 2012-2015 on 133 dogs presented with intestinal disorders. In order to assess the origin of the disorder, beside physical examination and biochemistry profile (total proteins, albumins, globulins, cholesterol), two other complementary imaging examinations were performed: ultrasound and endoscopic investigations. These investigations took place in two consecutive days, the first examination being the ultrasonography of the abdomen, followed the next day by the endoscopic examination so that any significant structural change could not appear after the start of the treatment. For both ultrasound and endoscopy, a twelve-hour fasting period was kept prior to investigation.

The inclusion criteria for this study provided that all dogs were referred by their practitioner presenting signs of intestinal disorder (diarrhea, weight loss, protein losing enteropathy) and were unresponsive to treatment. The cases that had not undergone both ultrasound and endoscopic examination or those with insufficient or low-quality images were excluded from the study. The images were examined and scored by 2 different pathologists, blinded to all patient data. Endoscopic samples were collected and the diagnosis of lymphangiectasia was established after histopathological examination.

Seventy-six cases met de inclusion criteria, represented by 36 males and 40 females. There were 27 nurtured males and 36 spayed females, with a median age for males of 8.1 years (range 0.8 – 12.1 years old) and of 6.8 years (1.4 – 11.8 years old) for females. The median weight was 17.7kg, with a range between 2.3 and 51.2kg. The most represented breeds (over 10 cases) were German Shepherds (17/76), Labrador Retrievers (13/26) and Cocker Spaniels (11/76). Other breeds examined in the study included Boxers, Yorkshire Terriers, Staffordshire Bull Terriers, Poodles, Huskies and common breed dogs. For each patient included in this study the written consent of the owner was obtained. All investigations respected UK national regulations in terms of animal management in clinical studies.

Laboratory data included determination of serum total proteins (TP), albumins, globulins and cholesterol. For each dog included in the study, a minimum of 5, high quality ultrasound and endoscopic images were required. Ultrasound examination used a Logiq 5 ultrasound machine with probes that have a frequency between 5 and 12 MHz. Ultrasound examination tried to assess the echogenicity changes of the intestines, changes in wall thickness, wall layering and presence of striations or / and speckles (hyperechoic structures along intestinal mucosal layer) (Delaney *et al.*, 2003). All of these changes were observed and quantified during the ultrasound examination by the clinician and also, by the two pathologists that examined both ultrasound and endoscopic images. The cases with inconclusive results after examination were not included in this study.

Endoscopic examination used an Olympus system, with Olympus CLV U40 light source and

Olympus CV 240 video system. The probes used were represented by pediatric Olympus GIF XP260 and Olympus GIF XP240 gastroscopes with a length of 1030mm, 6.5 to 7.7mm diameter of insertion tube, 2.0 to 2.2 diameter of working channel. Population characteristics such as weight and age were reported as medians and ranges. The data that was gathered has been statistically interpreted by two-tailed Fishers Exact Test to assess any significant correlations that would occur during the study and also Cohen's Kappa test to assess reliability of the study.

RESULTS

Serum biochemistry revealed decreased values for TP in 93.4% of cases, hypoalbuminemia (84.2%), hypoglobulinemia (56.6%) and hypocholesterolemia (57.9%). These results are in accordance with literature data (Rodriguez-Alarcon *et al.*, 2012). The median results for all patients are presented in Table 1.

Table 1. Serum biochemistry data for the patients with protein losing enteropathy and hypocholesterolemia (PLE)

Test	Cases	Unit	Median	Range	Reference*
Panhypoproteinemia	71	g/L	29.3	21-47	54-75
Hypoalbuminemia	64	g/L	13.7	9-16	23-31
Hypoglobulinemia	43	g/L	16.3	11-25	27-44
Hypocholesterolemia	44	mmol/L	1.5	0.9-2.7	3.5-7.2

*Merck Veterinary Manual. Online at: <http://www.merckvetmanual.com/mvm/index.html>.

Changes in normal echogenicity, as diffuse hyperechoic aspect at the level of duodenum or jejunum, were found in 63 dogs (82.9%), while 53 cases (69.7%) presented loss or alteration of specific wall layering mainly involving mucosa and submucosa layers. The duodenum wall was considered thickened if it exceeded the previously

published and validated results: <5.1mm (under 20kg); <5.3mm (20 - 29.9kg), <6.0mm (over 30kg) (Delaney *et al.*, 2003). Increased wall thickness was observed in 61 patients while localized lesions represented by the presence of striations was seen in 21 cases and speckles in 43 patients (Figure 1).



Figure 1. Mucosal layer of the small intestinal wall appears diffusely hyperechoic with echogenic speckles (arrow) – left, German Shepard, 9 years old; right, Labrador Retriever, 12 years old Endoscopic examination findings included dilated lacteals (59.2%) (Figure 2) and erythema (21.1%). Although increased friability was observed in 33 dogs, it has not been considered in the study due to limitations represented by the evaluation of the endoscopic images only.

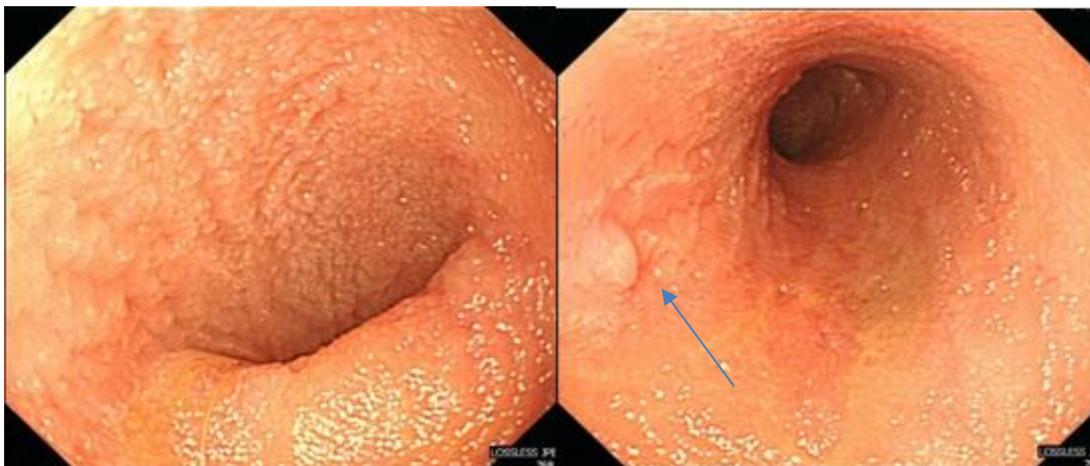


Figure 2. Lymphangiectasia – duodenum, dilated lacteals (arrow), white tipped villi. The histopathologic changes revealed that 57.9% of the patients were consistent with primary lymphangiectasia, the findings being considered primary inflammatory in 36.8% of the dogs, while 5,3% had neoplastic origin.

All 44 cases (57.9%) histopathologically diagnosed with lymphangiectasia presented dilated lacteals, and the presence of striations has been noted in 16 cases (36.4%), while speckles have been observed in 34 dogs (77.3%). Although changes concerning the echogenicity, thickness of the intestinal wall and loss or alteration of normal intestinal layering were observed in 72.7%, 61.4%, respectively 54.5%, these are not strictly consistent with lymphangiectasia, but rather are the result of inflammatory processes undergoing in studied individuals.

For the remaining 32 dogs (42.1%) with inflammatory and neoplastic lesions the endoscopic and ultrasound examination revealed the presence of dilated lacteals in just one case (3.1%), while striations and speckles were observed in 5 (15.6%), respectively 9 cases (28.1%). Thirty-four dogs had thickened intestinal wall, 31 revealed echogenicity changes and 29 patients presented wall layering loss. Cohen's Kappa test revealed moderate agreement between ultrasound and endoscopic findings in patients with lymphangiectasia, presenting both dilated lacteals and speckles ($k=0.42$).

DISCUSSION

The starting hypothesis of the study stated that no significant correlations occur between ultrasound and endoscopic findings in patients with lymphangiectasia which the study proved to be wrong. This research tried to assess the changes

that can be noticed under ultrasound and endoscopic examination. Prior to examination a twelve-hour fasting diet was kept, considering that some studies revealed that ingesting water or milk does not improve overall quality of the obtained images or even affect the view of mucosal layer (Webster *et al.*, 1997). More than that, milk ingestion associated with fermentation processes may induce production of gases which would make ultrasound examination more difficult.

Biochemistry revealed changes correlated to the presence of intestinal lymphangiectasia like hypoproteinemia and hypocholesterolemia. Hypocholesterolemia is attributed to gastrointestinal loss and lipid malabsorption. Although intestinal lymphangiectasia is responsible for lymph leakage into the bowel lumen, which also leads to lymphopenia, a total blood count was not performed. Considering that hypocalcemia is mainly an artifact of low serum albumin concentration, calcium levels have not been dosage even though it may be exacerbated by decreased intestinal calcium absorption.

This study describes specific ultrasound changes observed in patients with intestinal disorders, correlating these alterations with the macroscopic aspect of the intestinal mucosa in order to establish any significant associations between ultrasound appearance of a specific structure and its endoscopic image. In accordance to Sutherland-Smith *et al.* (2007), the mucosal

striations were associated with histological finding of lacteal dilation. All 21 dogs that presented striations also had dilated lacteals, however, less than 40% (36.4%) of the patients with lymphangiectasia revealed striations after ultrasound examination. Other sign observed in 72.7% of the dogs with lymphangiectasia was represented by speckles.

We consider that speckles represent sections through dilated lacteals which give characteristic hyperechoic aspect in ultrasound. The reason for the absence of speckles in the remaining 10 dogs (27.3%) may be represented by accumulation of mucus or other content in the intestinal lumen which may mask the lesions, as found by Sutherland-Smith *et al.* (2007). For the rest of 32 dogs without intestinal lymphangiectasia, a single case presented both dilated lacteals and speckles. There is an extremely significant statistical correlation between the presence of speckles and dilated lacteals in dogs with lymphangiectasia ($P < 0.05$). Up to now, there is no other study to make an association between the white spots observed in ultrasound examination and dilated lacteals revealed after endoscopy in dogs with intestinal lymphangiectasia.

The results support the hypothesis, correlating the presence of white spots in the duodenal mucosa to lacteals that are dilated and filled with chyle (German, 2005). In cases with intestinal lymphangiectasia, the intestinal villous dilate and become more fragile, and rupture easily (Melzer and Sellon, 2002), confirmed in our study by the increased friability of the intestinal mucosa (Malancus and Tofan, 2017). The predominant changes for the remaining 32 dogs confirmed without lymphangiectasia, were consistent with increased wall thickening, loss or alteration of the specific layering and changes to the normal intestinal echogenicity (Gaschen *et al.*, 2008; Malancus, 2015). These changes are specific to inflammatory (changes in echogenicity, diffuse wall thickening) or neoplastic lesions (localized wall thickening, loss of wall layering) (Penninck *et al.*, 2003).

Most of the patients (93.4%) complained protein-losing enteropathy, associated clinical signs including weight loss and diarrhea. Intestinal protein loss is a sign of digestive function failure that may result from severe acute or chronic inflammatory lesions or from a disruption of chyle

absorption and intestinal lymph flow. The exact mechanisms leading to intestinal protein loss have not been elucidated in the dog, but we take into consideration the leakage of protein rich lymph into the intestinal lumen as the main cause, with subsequent abnormal permeability and absorption related problems (Gaschen, 2013).

The most relevant changes encountered in patients with lymphangiectasia are better observed at the level of duodenum if we take into consideration both endoscopic and ultrasound findings. Statistical data reveal a specific correlation between ultrasound and endoscopic changes, although, in order to discuss the results in terms of reliability further studies may be conducted. Future research evaluating the correlation between ultrasound and endoscopic images in dogs with intestinal disease should include a blinded histopathological review of the cases, scoring all the encountered lesions and providing a standardized criterion of diagnosis for intestinal lymphangiectasia in dogs.

CONCLUSIONS

We consider that although endoscopy and ultrasound used alone for diagnosis of intestinal disorders in dogs have a moderate sensitivity, the data gathered using both imaging techniques provide an insight to the processes that develop inside the organism. Given the very significant association between the presence of speckles and dilated lacteals in dogs with intestinal lymphangiectasia, it is recommended to use both investigating techniques in patients expressing clinical signs associated with intestinal disorders in dogs.

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