

# Recurrent and multidrug-resistant suppurative mesenteric lymphadenitis in a dog

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**Citation:** Libarde MACA, Senhorello ILS. Recurrent and multidrug-resistant suppurative mesenteric lymphadenitis in a dog. Brazilian Journal of Case Reports. 2024 Oct-Dec;04(4): 65-72.

Received: 21 December 2023

Accepted: 31 March 2024

Published: 2 April 2024

**Abstract:** Suppurative mesenteric lymphadenitis is rarely described in veterinary medicine and is usually associated with other gastrointestinal or urinary tract diseases, immunosuppression, and infectious diseases. The aim of this study was to report a case of recurrent suppurative mesenteric lymphadenitis caused by coagulase-positive *Staphylococcus* in a 3-year-old female Shih Tzu dog, highlighting the importance of performing bacterial culture and antibiotic susceptibility testing for disease resolution. The animal was attended at the private Veterinary Hospital, in Vila Velha city, Espírito Santo, presenting clinical signs of abdominal pain in the hypogastric region, apathy, anorexia, and oligodipsia, along with a history of fever one day before and two similar episodes that were resolved with antimicrobial use. The patient had enlarged mesenteric lymph nodes and laboratory abnormalities consistent with an infectious process. Bacterial culture, following fine needle aspiration biopsy of the lymph nodes guided by ultrasound, identified the agent, and antibiotic susceptibility testing classified the bacterium as multidrug-resistant. The treatment instituted was meropenem combined with pain and fever control, leading to improvement of clinical signs, laboratory abnormalities, and disease remission. The patient did not experience recurrence, totaling 640 days of follow-up until the present time.

**Keywords:** Bacterial culture; Antibigram; Lymph nodes; Infection.



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## 1. Introduction

Mesenteric lymphadenitis is characterized by inflammatory involvement of intra-abdominal lymph nodes and has been reported in humans, pigs, cats, and dogs [1-8]. This inflammatory process can originate immunologically or infectious [6, 9]. When infectious, the main etiological agents are *Escherichia coli*, *Serratia marcescens*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Staphylococcus canis*, *Prevotella* sp., and more recently, *Salmonella enterica* [2, 5-8]. Furthermore, the disease can be caused by bacterial urinary tract infections, urolithiasis, ingestion of foreign bodies, traumatic injuries or ectopia, diffuse gastrointestinal inflammatory disease with bacterial translocation, sepsis, and peritonitis [6].

Case reports of dogs with a history of raw meat ingestion and subsequent development of mesenteric lymphadenitis due to *Salmonella enterica* have been published [7, 8]. The disease can also be classified as idiopathic when there is no history that allows for the classification of the infection's origin [6]. Despite being severe, the disease is considered rare in both veterinary and human medicine, and when reported, it appears as isolated cases [1, 6].

Once affected, animals present nonspecific clinical signs such as abdominal pain, fever, apathy, anorexia, diffuse pain, and exercise intolerance. In laboratory analyses, alterations related to systemic inflammation are observed [4, 6, 8]. Inflammatory leukogram with left shift, mild hypoalbuminemia associated with mild hyperglobulinemia, and hyperfibrinogenemia are reported. In urinalysis, the results may appear without apparent alterations or with results indicating infection or inflammation; however, in urine culture, in most cases, a negative result is obtained when the cause of lymphadenitis is not related to cystitis or pyelonephritis [5, 8].

Diagnosis is made through the perception of clinical symptoms combined with hematological exams and abdominal ultrasound. Additionally, fine needle aspiration of the affected lymph nodes along with cytological analysis, bacterial culture, and antibiotic susceptibility testing aid in defining the etiology of the disease [7, 8]. Treatment is based on the surgical removal of the affected lymph nodes, primarily indicated in cases where patients present with septic peritonitis or lymph node abscesses. A conservative approach can also be performed through the administration of antimicrobials [6-8].

This study aims to report the case of a dog that presented with recurrent and multi-drug-resistant mesenteric lymphadenitis, addressing clinical and laboratory signs, diagnosis, treatment, and prognosis.

## 2. Case Report

A 3-year-old, intact female Shih Tzu weighing 4.55 kg was presented to the small animal internal medicine department of a private veterinary hospital in Vila Velha, Espírito Santo, Brazil. During the consultation, the owner reported that the dog was lethargic, febrile (40°C), and had been anorexic for one day. The owner also mentioned that the patient had experienced a similar clinical condition twice, which coincided with periods after estrus. According to the medical records from previous visits, on both occasions, the dog received treatment with amoxicillin-clavulanic acid and metronidazole and required hospitalization.

The owner stated that the dog was fed with commercial dog food and occasionally consumed carrots and commercial pâtés. It was also reported that the dog's core vaccinations were not up to date, with only the rabies vaccine being current. The patient did not have access to the street, lived indoors, had contact with only one other dog, and was otherwise healthy. During the physical examination, the animal had a temperature of 38.7°C, normal hydration status, pink mucous membranes, a capillary refill time of 2 seconds, normal-sized peripheral lymph nodes, a heart rate within normal limits, but with tachypnea. Mild periodontal disease was noted upon oral cavity inspection. Additionally, abdominal palpation did not reveal pain, but there was galactorrhea upon mammary gland evaluation.

Given the presented symptoms, an initial suspicion of pseudopregnancy was raised. In this context, hematological and serum biochemical tests (complete blood count, urea, creatinine, alanine aminotransferase, alkaline phosphatase, proteins, albumin, and globulins) were requested. The animal was discharged for home treatment with a prescription of metergoline at a dose of 0.1 mg/kg/BID orally for 5 days and was advised to wear surgical clothing to prevent licking of the mammary glands. After 24 hours of the consultation, the requested tests were released, showing an increase in alkaline phosphatase (180 IU/L) and leukocytosis (19.100/ $\mu$ L) due to neutrophilia (13.179/ $\mu$ L).

One day after the initial consultation, the owner returned to the clinic complaining of worsening lethargy and reported oligodipsia. Additionally, complained that the dog had intense abdominal pain. During the physical examination, the patient had a temperature of 38.9°C, normal hydration status, pink mucous membranes, a capillary refill time of 2 seconds, normal heart and respiratory rates, normal-sized peripheral lymph nodes, and normal pulses. Additionally, abdominal palpation revealed pain in the hypogastric region, galactorrhea, and apathy. Based on this, a new complete blood count and

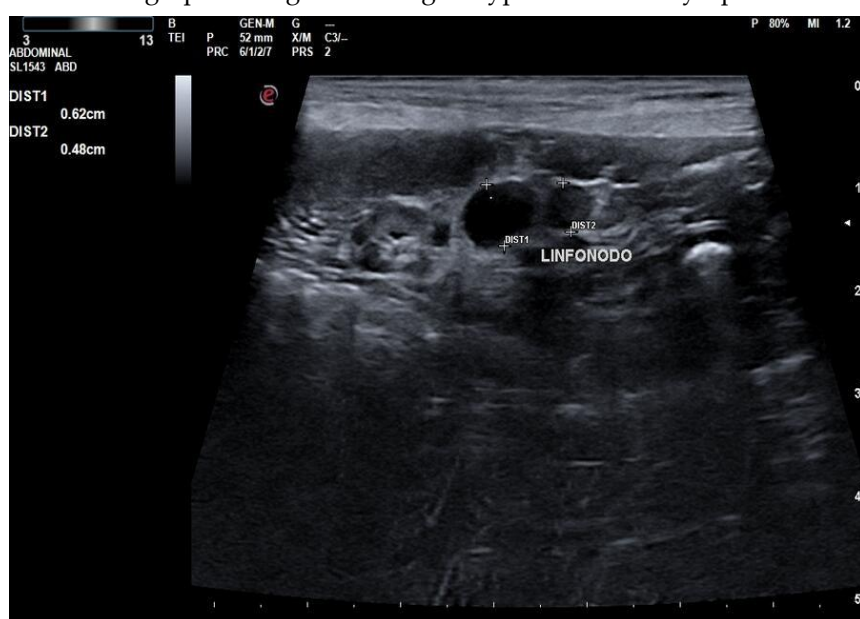
abdominal ultrasound were performed, suspecting a possible gastrointestinal infectious process, as the animal had a history of two similar episodes with abdominal pain and abdominal lymphadenopathy with an interval of approximately 1 year between them.

The complete blood count revealed normocytic normochromic anemia with a hematocrit value of 35%, 4.77 million/uL red blood cells, and 11.0 g/dL hemoglobin. Furthermore, there was an increase in leukocytes (30.500/uL) with regenerative left shift (610 band/uL) and thrombocytopenia (146.000/uL). The ultrasound findings were consistent with lymphadenopathy with multiple enlarged mesenteric lymph nodes (colic, jejunal, and gastric), with intense reactivity of adjacent fat, suggesting suppurative lymphadenitis (Figure 01 and Figure 02). The uterus was slightly enlarged with luminal fluid content. The animal also had moderate splenomegaly and hepatomegaly.

**Figure 1.** Ultrasonographic images of enlarged hypoechoic gastric lymph nodes.



**Figure 2.** Ultrasonographic images of enlarged hypoechoic colic lymph nodes.



Given the scenario, fine needle aspiration cytology of the affected lymph nodes was requested and scheduled for the following day. Bacterial culture and antibiotic

susceptibility testing of the collected material, as well as fungal culture, were also performed. Treatment with enrofloxacin (5 mg/kg 5 mg/kg every 12 hours orally) was initiated from the day of lymph node puncture until the results of the requested tests were available. Three days after starting the antimicrobial treatment, the results of the aspiration cytology revealed many neutrophils (intact and degenerated) and a moderate number of small lymphocytes, along with vacuolated macrophages, suggesting marked neutrophilic inflammation. The bacterial culture showed growth of coagulase-positive *Staphylococcus*. At this point, the antibiotic susceptibility results were not yet available, and the animal clinically deteriorated, showing lethargy, hyporexia, and fever, despite antibiotic therapy.

The laboratory tests continued to show worsening leukocytosis (41.800/uL) due to neutrophilia (31.350/uL) with left shift (836/uL band cells), as well as normocytic and normochromic anemia (erythrocytes: 4.22 million/uL; hemoglobin: 9.2 g/dL; hematocrit: 27%). In response, the antibiotic was changed to cephalexin (30 mg/kg every 12 hours orally), which was used for only two days since the antibiotic susceptibility results were released within that timeframe. The results revealed resistance to azithromycin, ciprofloxacin, norfloxacin, enrofloxacin, clindamycin, ceftiofur, ceftriaxone, cephalexin, oxacillin, metronidazole, amoxicillin/ clavulanic acid, and sulfamethoxazole/trimethoprim. The microorganism showed susceptibility only to imipenem, doxycycline, and gentamicin.. No growth of yeasts or other clinically significant fungi was observed in the fungal culture.

Given the results and the clinical deterioration of the patient, meropenem was initiated at a dose of 24 mg/kg every 12 hours intravenously in a hospital setting. On the day of the first administration, a complete blood count was performed, revealing a slight improvement in the anemic condition (erythrocytes: 4.65 million/uL; hemoglobin: 10.1 g/dL; hematocrit: 30.2%), but the leukocytosis (44.100/uL) persisted due to neutrophilia (38.808/uL) with a left shift (882/uL band cells).

The medication was administered for 7 consecutive days at a dose of 24 mg/kg every 12 hours intravenously, along with tramadol 4 mg/kg every 12 hours subcutaneously, and follow-up hematological tests were performed. Additionally, dipyrone 25 mg/kg every 12 hours intravenously in cases of fever was also prescribed. On the fourth day of administration, the complete blood count showed improvement in the anemic condition (erythrocytes: 4.61 million/uL; hemoglobin: 11.8 g/dL; hematocrit: 32.4%) and leukocytosis (30.000/uL) due to neutrophilia (22.200/uL) which at this point did not show a left shift. Additionally, lymphocytosis (6.600/uL) and thrombocytosis (549.000/uL) were observed.

The animal showed complete clinical improvement after the drug therapy. It returned for follow-up 27 days after the end of treatment, where complete resolution of laboratory and ultrasonographic abnormalities was observed. Up to the present moment, totaling 640 days, the animal remains in complete remission of the disease, with a favorable prognosis.

### 3. Discussion and conclusions

The case in question refers to a dog with recurrent and multidrug-resistant suppurative mesenteric lymphadenitis diagnosed through abdominal ultrasonography, lymph node cytology followed by bacterial culture, and antibiogram. Purulent mesenteric lymphadenitis and abscess formation are relatively rare findings. Over a period of 10 years in a university veterinary hospital, only 14 definitive cases were identified [6].

According to the literature, mesenteric lymphadenitis is defined as the inflammation of lymph nodes located in the intra-abdominal region [1]. This condition can be classified based on the predominant cell type in the lymph nodes. A higher number of neutrophils characterizes a suppurative process, consistent with the described case, while granulomatous lymphadenitis presents a higher number of macrophages. Pyogranulomatous conditions show the presence of both macrophages and neutrophils [9-10].

Cases of mesenteric lymphadenitis in dogs are rarely described in veterinary medicine, and as far as we know, there are no Brazilian publications on the subject [6-8]. A retrospective study conducted in 2016 with 14 dogs revealed a higher number of females (n=9) compared to males (n=5) among the affected patients. It was also noted that the animals had an average age of 3.4 years and average body weight of 19.9 kg [6]. In cats, mesenteric lymphadenitis has been reported in a series of 3 cases and in isolated cases [4, 5]. The data from the dogs in the study align with the sex and age of the patient in this report, and despite a relatively small number of animals, which limits conclusive data, the disease appears to be more common in young adult animals.

Other case reports in dogs have also shown a profile of young animals ranging from 7 months to 1 year old. The reported cases involved Golden Retrievers, German Shepherds, and Queensland Blue Heelers [7, 8]. The retrospective study spanning 10 years revealed that mixed-breed (SRD) and Small Munsterlander dogs were subjectively more represented compared to others, but due to the small number of animals, there is no certainty about breed predisposition [6]. The breed of the reported animal does not fit into the breeds mentioned in the studies, but it should be noted that due to the low caseload, it is not possible to define racial predisposition patterns.

The etiology of the disease can originate from immunomediated or infectious causes [6, 11]. Urolithiasis and urinary tract infections can be cited as triggers for the disease. Additionally, gastrointestinal inflammatory diseases such as gastroenteritis, presence of penetrating foreign bodies, and pancreatitis also predispose to the development of mesenteric lymphadenitis, as they lead to mucosal integrity loss and bacterial translocation. Systemic Inflammatory Response Syndrome (SIRS), sepsis, and peritonitis are often associated with lymphadenitis [12]. Intra-abdominal abscesses, caused by forgotten surgical materials in the cavity; traumatic organ injury; organ metaplasia; and ectopia also characterize factors that lead to the onset of the disease [6]. However, the patient had not undergone surgical procedures or trauma prior to the diagnosis of lymphadenitis. Furthermore, she did not present autoimmune diseases, gastrointestinal disorders, or urinary tract diseases. Therefore, it was not possible to identify the underlying cause of the disease, classifying it as idiopathic.

Nevertheless, it is noteworthy that the patient in question presented clinical signs during diestrus periods. This period is characterized by increased serum levels of progesterone in the female's body [13]. It is known that progesterone plays an important role in decreasing cellular immunity [14]. Given this, it is believed that the decrease in immune capacity during diestrus may have contributed to suppurative mesenteric lymphadenitis.

During the physical examination, it was noted that the patient had fever and intense abdominal pain. Furthermore, during the anamnesis, the owner reported hyporexia and apathy. Studies describe abdominal pain and fever as the most common clinical signs in affected humans and animals [1, 6]. In addition, anorexia, lethargy, weakness, exercise intolerance, and in some cases vomiting and diarrhea are also reported [1, 5, 6].

The diagnosis of the patient was made as described in the literature through the combination of clinical signs, hematological laboratory findings, abdominal ultrasonography, fine-needle aspiration cytology of the affected lymph nodes, bacterial culture of the collected material, and antibiogram [1, 8]. Urinalysis can also be performed to identify possible urinary tract infections [6], but it was not conducted in this case due to the absence of clinical signs in the urinary tract, as well as no abnormalities in the ultrasound imaging.

In the complete blood count, the main alteration observed was leukocytosis with neutrophilia, which may also present monocytosis [6, 7]. Left shift and elevated C-reactive protein were repeatedly observed during hematological evaluation of the studied patients [1, 6]. In the laboratory findings of the patient in this case, normocytic normochromic anemia, leukocytosis with regenerative left shift due to neutrophilia and lymphocytosis, as well as thrombocytopenia, were observed. However, monocytosis was not observed. The C-reactive protein test was not performed.

In serum biochemistry tests of the patient, an increase in alkaline phosphatase was observed as the only alteration. However, biochemical tests were performed only once during the initial assessment, with no repetitions throughout the diagnosis and treatment. The literature reports that cases involving hepatobiliary involvement may show mild hyperbilirubinemia and elevated alkaline phosphatase [6]. The patient presented hepatomegaly in ultrasound findings but no abnormalities in the gallbladder. Bilirubin was not requested as a complementary test. In a case of mesenteric lymphadenitis in a dog, described in 2020, mild hypoalbuminemia and mild hyperglobulinemia were observed as biochemical alterations [7]. This alteration was also found in the dogs evaluated in the retrospective study [6]. However, these were not found in the tests of the patient in this report.

Regarding complementary imaging tests, ultrasound is considered the main diagnostic method in both veterinary and human medicine [1, 6, 8]. Published data reveal ultrasonographic aspects of lymphadenitis including enlarged lymph nodes, reduced echogenicity, and a homogeneous appearance with poorly defined borders [1, 7]. However, in some cases, they can appear heterogeneous with cavitations [8]. The ultrasound findings of the patient corroborate with characteristics of hypoechoic appearance, increased size, and evident vascularity with intense reactivity of adjacent fat. The lymph nodes had rounded shapes with regular borders.

Fine-needle aspiration cytology is a valuable diagnostic test to investigate the cause of lymph node enlargement due to its low cost, simplicity, and rapid results [15]. Therefore, it was the method of choice for this case.

The main bacterial etiological agents of the disease include *Escherichia coli*, *Serratia marcescens*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Staphylococcus canis*, and *Prevotella* sp. However, infections by *Salmonella* spp. have also been described in dogs, although they are more common in humans [1, 6-8]. In the present case, bacterial culture revealed growth of coagulase-positive *Staphylococcus*, as already described in the literature. Bacterial resistance to several active ingredients was also observed, with sensitivity only to imipenem, doxycycline, and gentamicin. It is worth noting that the patient had a history of two episodes with the same symptomatology and laboratory results and was subjected to treatments using amoxicillin and metronidazole empirically, which may have contributed to the selection of multidrug-resistant bacteria.

In this context, a retrospective study evaluating dogs and cats that received antibiotic therapy in 2021 at the Prof. Ricardo Alexandre Hippler Veterinary Hospital of Vila Velha University-ES, showed the use of antibiotics linked to empirical practices and the absence of bacterial culture and antibiogram as preliminary exams for choosing antibiotics. Among the most used drugs were amoxicillin with potassium clavulanate and metronidazole, the same ones used to treat the dog in this study [16].

Despite the association of these medications covering a broad spectrum of bacteria, their use without prior isolation and identification of the causative agent of the infectious condition predisposes to bacterial multidrug resistance, as well as intestinal microbiota destruction, drug intolerance, leading to treatment failure [17].

The treatment of mesenteric lymphadenitis can be done conservatively with antibiotics or through surgical intervention, based on the excision of the affected lymph node(s). The duration of antibiotic treatment has not been defined yet. In cases of septic peritonitis or lymph node abscesses with a risk of rupture, surgery is more indicated as it yields better long-term results [6, 8]. The reported patient, however, did not present peritonitis, free fluid, or lymph node abscesses in ultrasound findings; therefore, antimicrobial therapy was initiated without surgery.

Among the most used antibiotics in the retrospective study are amoxicillin with clavulanate alone or in combination with enrofloxacin [5]. However, despite the use of these antibiotics in a greater number of animals, it is crucial to highlight the importance of bacterial culture in conjunction with antibiogram examination, as it helps the clinician make more accurate decisions, rationalizing drug use and increasing the chances of

resolving infectious conditions [17]. The animal reported in this study only showed clinical improvement after administration of the antibiotic to which the bacterium found was sensitive according to the antibiogram.

In a report of two dogs diagnosed with mesenteric lymphadenitis caused by bacterial agent (*Salmonella* spp.), the choice of antimicrobials to be used during treatment was based on antibiogram results [6]. The mentioned dogs responded satisfactorily to treatment and recovered from the disease, highlighting the importance of this examination in decision-making. In another recent report, culture and antibiogram were essential for determining appropriate therapeutic management [8].

The dog in this case was subjected to conservative treatment using antibiotics only, combined with supportive treatment for pain and fever control. Based on the results evidenced by the antibiogram, it was found that the use of enrofloxacin and cephalexin would not be effective for resolving the condition, and there was a need to change these medications. The administration of meropenem was the only effective therapy for this condition. Although doxycycline and gentamicin were identified by the antibiogram as effective drugs against the agent, they were not used due to their bacteriostatic and nephrotoxic factors, respectively [18, 19].

After treating the disease, some animals may experience recurrence of the condition. In the single retrospective study conducted, three animals had relapses from 3 to 4 months after treatment. They showed similar clinical signs to those identified during the first episode. However, these animals were subjected to conservative treatment using antibiotics and responded well [6]. The patient in this case, on the other hand, experienced two recurrences and after the last treatment is in complete remission of the disease. To date, the animal is healthy and shows no signs of lymphadenitis recurrence, being 640 days free from the disease.

From the reported case, it is emphasized that despite the low incidence of suppurative mesenteric lymphadenitis in dogs, the disease should be investigated in cases of abdominal pain associated with fever, anorexia, oligodipsia, and apathy. Moreover, laboratory tests involving findings suggestive of infection and inflammation reinforce the need for abdominal ultrasonography and fine-needle aspiration cytology in cases of lymphadenomegaly, aiming to identify the causative agent through bacterial and fungal culture.

The present case highlights the importance of antibiogram for the accurate choice of antimicrobials and resolution of the clinical condition, as the patient's disease had a recurrent and multidrug-resistant nature. Once an effective systemic antibiotic against the agent was instituted, clinical and laboratory improvement was achieved without disease recurrence. The use of empirical antibiotics in both previous treatments may have led to multidrug resistance of the causative agents of lymphadenitis.

**Funding:** None.

**Research Ethics Committee Approval:** None.

**Acknowledgments:** None.

**Conflicts of Interest:** None.

**Supplementary Materials:** None.

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