Case Report

Cervical Lymphangiosarcoma in a Poodle Dog: Surgical Treatment and Chemotherapy

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Abstract

A 7-year-old neutered male Poodle exhibited a persistent caudoventral cervical mass with draining lesions characterized by chronic and relapsing features. Upon presentation, the mass measured 7 × 11 × 11.5 cm, containing sanguine fluid. Computed tomography revealed the diffuse extension of the cervical mass from the C3 level to the thoracic inlet, affecting the sternal lymph node. Extensive surgical removal was attempted with meticulous resection to avoid damaging the right jugular vein, carotid sheath, and vagus nerve within the mass. Histopathology and immunohistochemical staining for factor VIII confirmed the diagnosis of lymphangiosarcoma. Due to inadequate surgical margin excision, four cycles of doxorubicin chemotherapy were administered starting from postoperative day 11. However, a local recurrence of the 3-cm mass occurred at 10 weeks postoperatively. Despite ongoing chemotherapy, fluid accumulation progressively increased, and the patient succumbed to the condition 4 months after the operation.

Keywords: cervical mass, computed tomography, dog, doxorubicin, lymphangiosarcoma

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Introduction

Lymphangiosarcoma, a malignant neoplasm originating from the endothelium of lymphatic vessels, is a rarely documented condition in dogs. Typically, its initial presentation involves a subcutaneous mass or edema filled with serosanguinous fluid, often misinterpreted as a secondary infection or a chronic nonhealing wound (Williams, 2005). This diagnostic confusion frequently leads to the identification of metastasis at the time of the initial diagnosis (Fossum *et al.,* 1998; Sicotte *et al.,* 2012).

The prognosis of lymphangiosarcoma is guarded, primarily due to the tumor's aggressive nature, characterized by rapid growth, disease progression, widespread metastasis, and limited responsiveness to therapeutic interventions (Barnes *et al.,* 1997). Originating in the subcutaneous tissue, lymphangiosarcoma rapidly infiltrates underlying muscles and surrounding soft tissues, occasionally metastasizing (Williams, 2005). Various reported therapeutic approaches include surgical excision alone or a combination of surgery with chemotherapy and/or radiation therapy (Curran *et al.,* 2016). However, due to the scarcity of cases, the superiority of a specific treatment regimen has not been conclusively established.

This case report outlines the clinical, pathological, and immunohistochemical characteristics of cervical lymphangiosarcoma in a dog that underwent surgical intervention and chemotherapy.

Case description

A 7-year-old neutered male toy poodle dog weighing 6 kg presented with a caudoventral cervical mass that had been persisting for a year. The patient had previously undergone surgical excision of the mass and multiple drainages over a year at another hospital. Despite these efforts, the mass consistently recurred, displaying continuous fluid accumulation and progressive enlargement. Consequently, the patient was referred to our hospital.

No specific findings were noted at the time of presentation except for a caudoventral cervical mass measuring 7 × 11 × 11.5 cm (Fig. 1a) on physical examination. The aspirated fluid from the mass showed sanguineous characteristics, and cytological examination revealed mild inflammation, primarily consisting of small lymphocytes, along with the presence of neutrophils and macrophages without evidence of an infectious agent. There was no remarkable finding in hematology. Clinical chemistry revealed elevated alanine aminotransferase (302 U/L; reference interval [RI], 10–125 U/L), elevated alkaline phosphatase (1,899 U/L; RI, 23–212 U/L), mild hyperproteinemia (8.3 g/dL; RI, 5.2–8.2 g/dL), and mild hypophosphatemia (2.3 mg/dL; RI, 2.5–6.8 U/L). Endocrine tests revealed slightly reduced levels of total thyroxine (0.89 µg/dL; RI, 1.3–3.5 µg/dL) and pre- and post-ACTH hypocortisolemia (pre-ACTH sample, <1.0 µg/dL; range, 1.0–6.0 µg/dL; post-ACTH sample, <1.1 µg/dL; range, 5.5–20.0 µg/dL). Complete blood count and blood gas analysis fell within the reference intervals, and urinalysis results were unremarkable.

Thoracic and abdominal radiographs and an abdominal ultrasound examination showed no remarkable findings. Ultrasound revealed an extensive mass extending from the right cervical area to the sternum, characterized by abundant internal vascularity, the presence of cystic spaces, and signs of cellulitis. Computed tomography demonstrated that the right cervical mass, located within the interfascial plane between subcutaneous tissue and musculature, extended from the C3 vertebral level to the thoracic cavity (Fig. 2). The origin of the mass was identified as the right prescapular lymph node. The intramass features primarily exhibited a hypoattenuation pattern without significant contrast enhancement. An inflammatory reaction was evident in the perimuscular tissue adjacent to the mass, with both the right external jugular vein and the right cephalic vein traversing through the mass. Although the left prescapular lymph node displayed normal morphology, lymphadenopathy was observed in the right medial retropharyngeal and sternal lymph node. Notably, a suspected metastatic nodule, measuring 3 mm in diameter, was observed in the right anterior lobe of the lung. Regarding the assessment of abdominal organs, no abnormalities were detected except for the presence of a hepatic cyst.

An extensive surgical procedure was performed to achieve histopathological information and reduce the mass size (Fig. 3). Prior to the surgery, the fluid within the cysts was thoroughly aspirated, confirming a hemoserous exudate consistent with the initial assessment. The patient was positioned ventrodorsally with the forelimbs extended caudally and the neck extended. A skin incision was made from the C2 level to just in front of the right shoulder joint. Subsequently, a visual assessment was conducted to ensure the integrity of the jugular vein, esophagus, trachea, recurrent laryngeal nerve, carotid artery, and vagus nerve. Multiple cysts were identified in various locations, creating deep empty spaces and hematomas between tissues. All previous subcutaneous sutures were removed, and anomalous structures surrounding the sternocephalicus and sternohyoid muscles were carefully separated. One of these structures was entwined around the jugular vein, which was excised without causing them harm.

Moreover, the artery supplying blood to the mass, as identified on the CT scan, was located, ligated, and surgically removed. After confirming the absence of active bleeding, the surgical area was thoroughly irrigated with saline solution multiple times. The extensive empty space was closed using the walking suture technique. Two 6 French Penrose drain tubes were inserted at separate sites, and the skin margin was trimmed and sutured. The patient experienced postoperative facial edema, which resolved within 5 days. The Penrose drain tube was removed on the 11th postoperative day as the exudate decreased to 1–2 ml/kg/day or less, and the surgical site exhibited good healing (Fig. 1b).

Histopathological examination, using hematoxylin and eosin staining and immunohistochemical staining for factor VIII, confirmed the presence of lymphangiosarcoma. The subcutaneous mass showed an unencapsulated and infiltrative neoplasm

consisting of pleomorphic neoplastic cells supported by bundles of hyalinized collagen (Fig. 4). There was mild anisocytosis and anisokaryosis, with a low mitotic index (1 per 10 high-power field). Additionally, a focal suture granuloma was present, displaying adjacent granulomatous inflammation and osseous metaplasia.

Due to the aggressive nature of the tumor and insufficient surgical margin, chemotherapy was initiated with doxorubicin (30 mg/m^2 IV every 3 weeks) 11 days after surgery. However, by the third dose of doxorubicin, a local recurrence of the mass with fluid accumulation, measuring 3.5 cm, was identified (Fig. 1c). Despite good tolerance to the five intravenous doxorubicin treatments with no notable side effects, there was a continuous increase in tumor size. The owner refused further anticancer treatment, and the patient was managed with repeated drainage and bandaging. Unfortunately, the patient died suddenly 4 months after the operation.



Figure 1 Gross lesion of the cervical lymphangiosarcoma in a dog. At presentation (A) and 13 days post-surgical removal (B). A newly developed mass, approximately 3.5 cm in diameter, recurred 74 days after surgery (C).

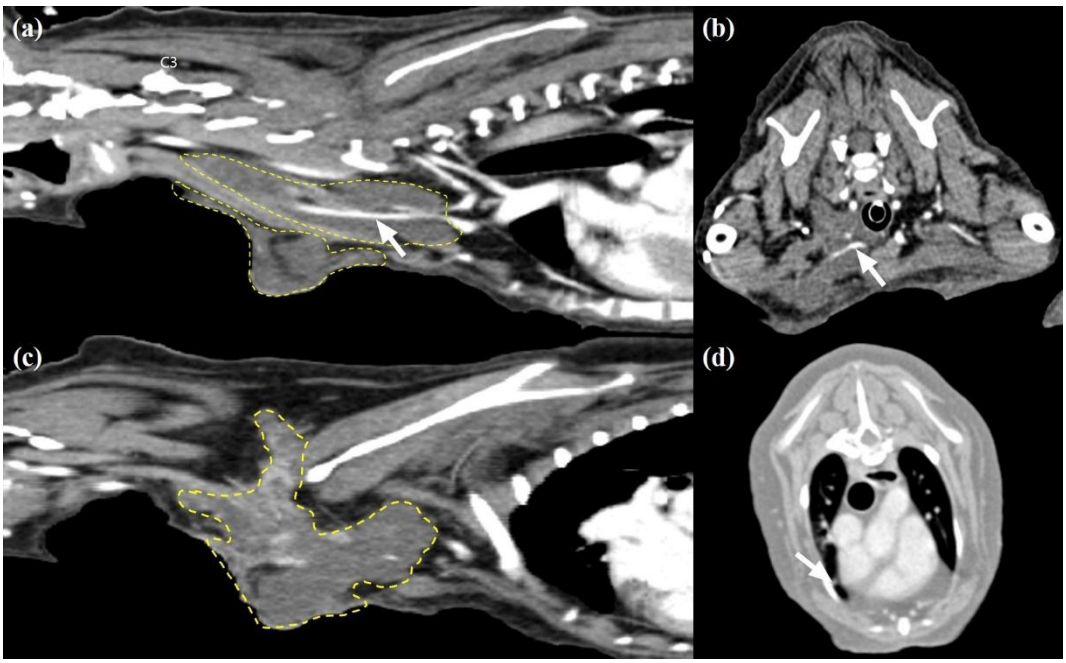


Figure 2 Computed tomographic findings of the mass. The right cervical mass, thought to originate from the right prescapular lymph node, extends from the C3 vertebral level to the thoracic cavity (A and C, dotted lines). The right external jugular vein (A, arrow) and right cephalic vein (B, arrow) traverse within the mass, and a suspected lung metastasis nodule was observed in the right anterior lobe of the lung (D, arrow).

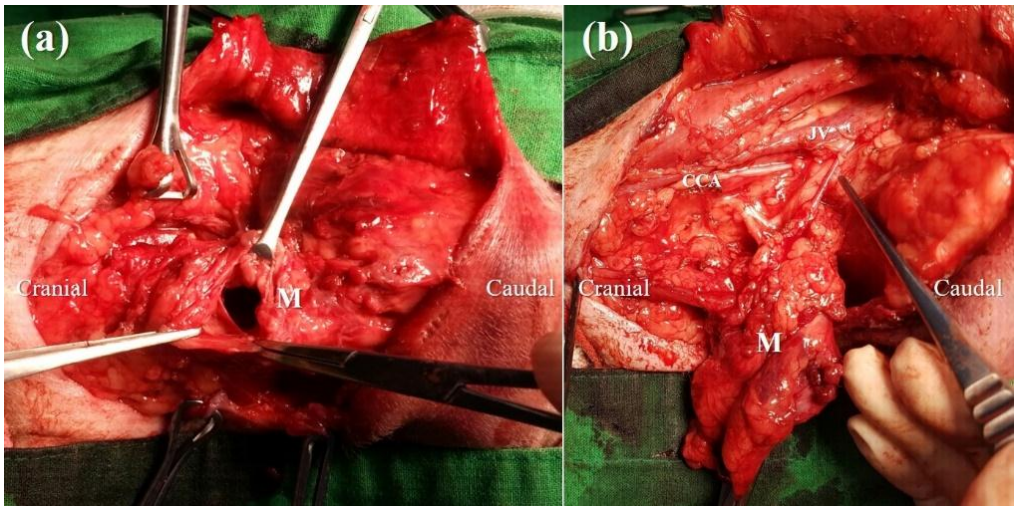


Figure 3 Left lateral view of the surgical site. The patient was positioned in ventral recumbency with neck extension. Multiple cystic structures within the mass created extensive dead spaces (A). The mass, challenging to distinguish from surrounding tissues and lacking a defined shape, was excised while preserving adjacent major structures (B). M, mass; JV, jugular vein; CCA, common carotid artery.

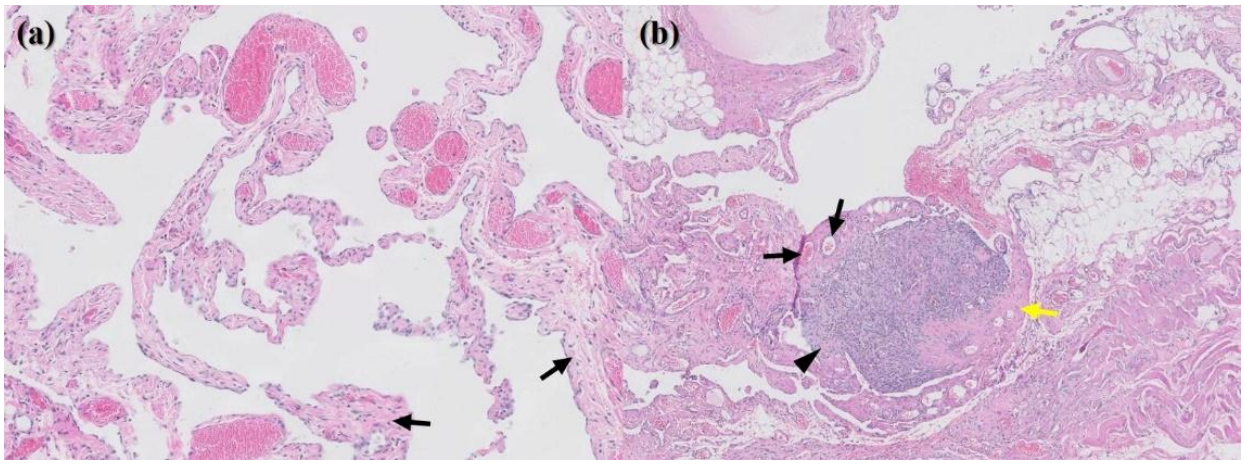


Figure 4 Histopathological section of the cervical lymphangiosarcoma. (A) The infiltrative neoplasm comprises spindle-shaped tumor cells, variably sized vascular spaces that are often empty or contain a small amount of blood, with bundles of hyalinized collagen (black arrows) (hematoxylin and eosin staining ×400). (B) Focal suture granuloma (black arrows), moderate granulomatous inflammation (black arrowhead), and osseous metaplasia (yellow arrow) were identified adjacent to the mass (hematoxylin and eosin staining ×200).

Discussion

Lymphangiosarcoma primarily affects medium- to large-breed dogs, typically appearing between 8 weeks and 13 years (Williams, 2005). Its occurrence in small breed dogs is exceptionally rare, with only one documented case reporting mediastinal lymphangiosarcoma in a toy Poodle dog with respiratory symptoms (NC3rd *et al.*, 1996). This case involves a Poodle dog with cervical lymphangiosarcoma that extended into the thoracic cavity, presenting with recurring skin swelling and draining lesions. Lymphangiosarcoma commonly manifests as progressive subcutaneous edematous or draining lesions without an apparent cause, often leading to delayed diagnosis due to repeated wound management (Curran *et al.*, 2016). In this presented case, the history showed prolonged symptoms with no improvement despite repeated wound management and surgical debridement over 1 year at the referring hospital. Endocrine assessments revealed iatrogenic hyperadrenocorticism and a mild decrease in total T4, likely due to the long-term use of corticosteroids, which might have hindered wound healing and caused skin thinning (Lux, 2022). Although the relationship between the duration of symptoms before diagnosis and survival time remains unclear, the tumor demonstrates rapid spread and invasion of surrounding tissues (Barnes *et al.*, 1997; Seo *et al.*, 2021; Shiga *et al.*, 1994). Furthermore, metastasis to the lungs or mediastinum occurs, contributing to an unfavorable prognosis (NC3rd *et al.*, 1996; Waldrop *et al.*, 2001; Williams, 2005). A CT scan conducted upon the initial presentation to our hospital revealed an invasion of the sternal lymph nodes through the thoracic cavity, with confirmed metastasis to the lungs.

This patient received a diagnosis of lymphangiosarcoma based on histopathological characteristics and the positive immunohistochemical staining for factor VIII-related antigen. Notably, the presence of adjacent granulomatous inflammation with partial suture encapsulation around neoplastic cells provided evidence of prior surgical resection,

along with osseous metaplasia indicating degenerative changes. Immunohistochemical markers for the vascular endothelium, such as factor VIII-related antigen and CD31, were positive in lymphangiosarcoma cells (Vail *et al.,* 2019). To distinguish it from hemangiosarcoma, the use of more specific labels for lymphatic endothelium, namely, lymphatic vessel endothelial receptor-1 (LYVE-1) and prospero-related homeobox gene-1 (PROX-1), is recommended (Cook *et al.,* 2021). However, their routine application in general veterinary diagnostic laboratories is limited due to their current restricted availability.

Recently, a feline case illustrated complete remission achieved through prompt surgical resection, but the available evidence supporting a complete cure through early-stage surgical intervention in dogs is insufficient (McInnis *et al.,* 2023). Previous studies have shown that, while not all surgically treated dogs achieved complete surgical margins, incorporating surgery, either alone or in combination with radiation or chemotherapy, resulted in the longest survival times among the dogs (Curran *et al.,* 2016; Itoh *et al.,* 2004). In our case, the surgical procedure presented challenges in defining precise boundaries and obtaining sufficient margins due to adjacent critical anatomical structures. This complexity may be inherent to the tumor's characteristics or could have been exacerbated by previous surgical interventions, as evidenced by visible suture knots and granulomas from prior surgeries surrounding and within the tumor. A preoperative CT scan indicated that complete tumor excision was unfeasible, leading to primary surgery aimed at precise diagnosis through histopathology and reducing tumor size before initiating adjuvant therapy. In previous research, more than half of surgically treated dogs experienced surgical site dehiscence (Curran *et al.,* 2016). Although our patient did not encounter this complication, the drainage tube removal was delayed compared to patients using drainage tubes for general dead space due to the notably slow reduction in drainage volume.

Surgical resection of lymphangiosarcoma often results in incomplete margins and rapid recurrence postoperatively, prompting consideration of adjuvant therapies like chemotherapy or radiotherapy (Curran *et al.,* 2016). While doxorubicin has demonstrated effectiveness in some reports, ensuring no recurrence before completing doxorubicin cycles, its efficacy in this particular case was limited (Curran *et al.,* 2016; Marcinowska *et al.,* 2013). The period without recurrence lasted approximately 2 months, with local recurrence observed 74 days after surgery. Given the advanced invasion of surrounding lymph nodes and lung metastasis at the time of diagnosis, it is hypothesized that there are limitations in responsiveness to both surgical resection and chemotherapy.

Information regarding the efficacy of postoperative chemotherapy or radiotherapy is scarce due to the rarity of the tumor. Reports have suggested transient responses or ineffectiveness with doxorubicin treatment followed by metronomic cyclophosphamide or chlorambucil (Curran *et al.,* 2016; Marcinowska *et al.,* 2013). Toceranib phosphate, a tyrosine kinase inhibitor, led to almost complete regression in a dog with recurrent lymphosarcoma resistant to rescue therapy using chlorambucil and meloxicam after doxorubicin chemotherapy (Marcinowska *et al.,* 2013). Another case demonstrated the effectiveness of toceranib phosphate, prednisolone, and benzopyrone in a 4-month-old puppy with lymphangiosarcoma associated with lymphedema (Kim *et al.,* 2018). However, lymphangiosarcoma with lung metastasis in dogs is extremely rare, and cases with a confirmed favorable prognosis are often limited to invasion of surrounding tissue or regional lymph node metastasis (Curran *et al.,* 2016; Itoh *et al.,* 2004). Currently, there is a lack of research on the prognosis or treatment responsiveness of lymphosarcoma accompanied by pulmonary metastases. Given the limited response to doxorubicin in this case, aggressive treatments such as surgery, multimodal chemotherapy, and radiation therapy may need to be considered in patients with confirmed distant metastases at the time of diagnosis. Further investigation is warranted to explore various treatment options for canine lymphosarcoma.

The patient in this case experienced sudden death 4 months after surgery, and a necropsy could not be conducted due to the owner's refusal. In a previous retrospective study involving 12 dogs with lymphangiosarcoma, 5 succumbed to disease progression and 5 died for reasons unknown (Curran *et al.,* 2016). The absence of postmortem examination results in a lack of precise information on the exact cause of death in canine lymphangiosarcoma. However, a previous study reported metastases to abdominal organs, lung parenchyma, and thoracic hemorrhage observed during necropsy (Barnes *et al.,* 1997). In this case, no complications related to doxorubicin were identified; however, considering that distant metastases were confirmed at the time of diagnosis, the cause of death was attributed to disease progression.

In conclusion, we described the clinical and histopathological characteristics and clinical course of lymphangiosarcoma in the cervical region in a poodle dog. For focal swelling with chronic non-healing wounds in small breed dogs, lymphangiosarcoma should be considered to avoid delaying the diagnosis. In addition, considering the poor responsiveness of doxorubicin in lymphangiosarcoma with distant metastases, further research on new anticancer treatment options is needed.

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