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CASE REPORT
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Tonsillar Squamous Cell Carcinoma in a Dog: Therapeutic Effects of Carboplatin Alone and Adjuvant Piroxicam

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ABSTRACT

***Background*:** Primary tonsillar neoplasia in dogs is rare, and among these tumors, tonsillar squamous cell carcinoma (SCC) is of particular concern because of its aggressive biological behavior, high metastatic rate, and generally poor prognosis. Reported treatment strategies for this include surgery, chemotherapy, radiation therapy, and non-steroidal anti-inflammatory drugs (NSAIDs). However, the optimal therapeutic approach remains undefined, and data regarding the efficacy of systemic chemotherapy as a single modality are limited. This report describes the clinical course and outcome of a dog with advanced tonsillar SCC managed with carboplatin in combination with adjuvant piroxicam.

***Case*:** A 14-year-old castrated male Mongrel dog was evaluated for anorexia, lethargy, and bilateral cervical masses. Physical examination and ultrasonography identified marked enlargement of the bilateral medial retropharyngeal and right submandibular lymph nodes (LNs), as well as a hypoechoic nodule in the spleen. Fine needle aspiration of both the lymph nodes and the splenic lesion revealed malignant epithelial cells. Computed tomography further demonstrated a right tonsillar mass consistent with a primary tumor, supporting a diagnosis of tonsillar SCC with concurrent lymph node and splenic metastases. The patient underwent 7 cycles of carboplatin chemotherapy (179.4-207 mg/m^2, intravenous, every 3 weeks) administered concurrently with oral piroxicam (0.3 mg/kg, once, daily). Following the initial cycle, the dog exhibited rapid improvement in clinical signs, including resolution of anorexia, lethargy, and weight loss. Serial physical examination and imaging demonstrated a partial response, characterized by substantial reduction in the cumulative size of metastatic lymph nodes and complete resolution of splenic metastasis although the primary tonsillar lesion remained stable in size. After the 7th carboplatin cycle, the dog developed severe neutropenia accompanied by gastrointestinal signs, prompting discontinuation of chemotherapy at the owner's request. Palliative management with piroxicam alone was continued, but progressive lymphadenopathy and worsening clinical symptoms ensued. The patient was transitioned to hospice care and died at home 53 days after cessation of chemotherapy, surviving 208 days from the time of diagnosis.

***Discussion*:** This case highlights several important clinical considerations in the management of canine tonsillar SCC. Although regional lymph node involvement is common, the occurrence of splenic metastasis is rare, underscoring the importance of comprehensive diagnostic staging in patients with suspected primary tonsillar tumors. While multiple treatment modalities are available, including surgery and radiation therapy, no single strategy has been shown to consistently improve long-term outcomes, particularly in cases with advanced local invasion or metastasis where local therapies are of limited benefit. In this patient, the combination of carboplatin and piroxicam achieved meaningful clinical improvement, prolonged survival, and control of metastatic lesions in the absence of surgery or radiotherapy. These findings suggest that carboplatin, when administered alongside NSAID therapy, may provide therapeutic benefit in selected cases of advanced canine tonsillar SCC. Further studies are warranted to establish the efficacy, safety, and optimal role of chemotherapy and adjunctive agents in the management of this aggressive neoplasm.

Keywords: dogs, neoplasia, oropharyngeal tumor, carboplatin, chemotherapy, piroxicam.

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INTRODUCTION

In dogs, primary tonsillar neoplasia is rare, accounting for 8%-25% of all oropharyngeal tumors, [1,5,10] and oral squamous cell carcinoma (SCC) is the 2nd most common malignant oral tumor, with caudally-located lesions exhibiting more aggressiveness [17]. Compared with other SCC sites, tonsillar SCC is associated with high metastasis and poor prognosis rates [12]. Its clinical signs include unspecific symptoms like lethargy, anorexia, weight loss, and respiratory symptoms because of the mass effect in the tonsils.

Incidental cervical masses from LN metastasis are also frequently observed [7,9]. This disease is considered systemic at diagnosis in more than 90% of affected dogs and cats, and most cases have metastasis at the time of detection [3,14]. Treatment options include surgery, chemotherapy, radiation therapy, and non-steroidal anti-inflammatory drugs (NSAIDs). However, the most effective treatment is unclear. Although chemotherapy may delay tonsillar SCC metastasis, its role remains under investigation [2,9,11,15].

Information about which chemotherapy drug is the most effective, as well as the efficacy of chemotherapy alone, remains limited. In this case, a dog diagnosed with tonsillar SCC received carboplatin chemotherapy alone and adjuvant piroxicam without any local treatment. The patient survived for 208 days after diagnosis while exhibiting a more favorable prognosis when compared with previous studies involving chemotherapy alone [15]. This report suggests that combining carboplatin and piroxicam has therapeutic efficacy for canine tonsillar SCC management.

CASE

A 14-year-old castrated male mongrel dog, weighing 4.85 kg, was referred to our hospital with lethargy, anorexia, and palpable cervical masses. One month earlier, the dog had been presented at a local hospital with anorexia and lethargy. Despite treatment with antibiotics and fluid therapy, the clinical signs worsened, with elevated C-reactive protein levels. The cervical masses became palpable two days before referral.

A physical examination at the initial presentation revealed enlarged, firm, and immobile bilateral cervical masses. The right mass was round and measured 56 × 43 mm, while the left mass was elongated and oval-shaped, with a long diameter of 23 mm (Figure 1). The masses were palpated without pain and fever. The submandibular LNs were indistinctly palpated by the cervical masses, and other superficial LNs appeared normal. The dog also had lethargy, tachycardia (200 beats per minute), dehydration (6%), a rectal temperature of 39.6°C, and a body condition score of 2/9. Auscultation revealed a grade 4 heart murmur.

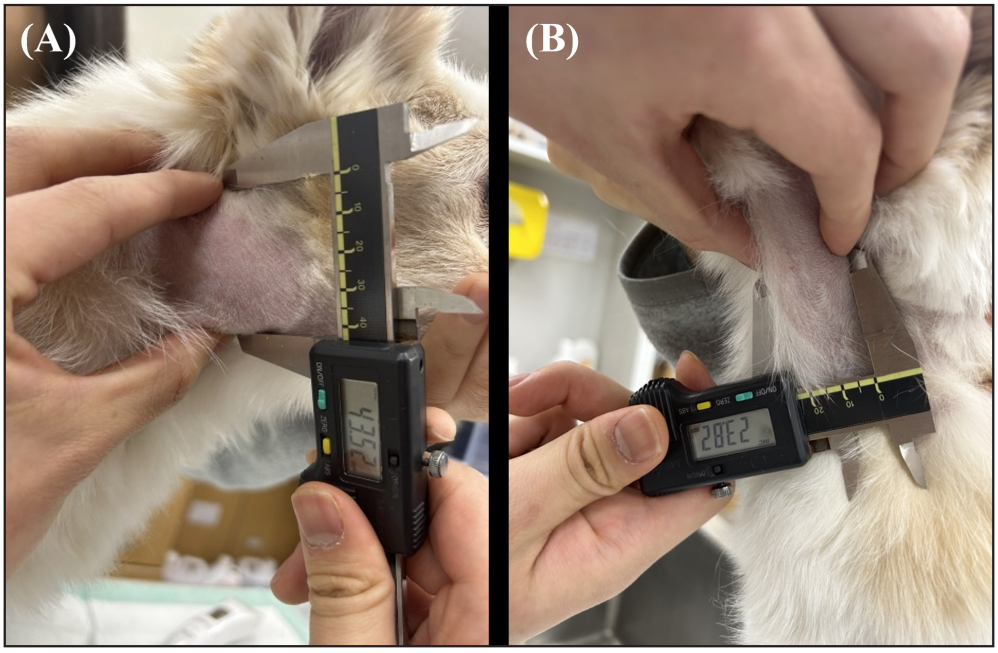

Figure 1. Bilateral cervical masses at 1st presentation. A- The right cervical mass was round, measuring 56 × 43 mm. B- The left mass was elongated and oval-shaped, with a maximal diameter of 23 mm.

Complete blood count and biochemistry panel results were within reference ranges, except for elevated alkaline phosphatase (1010 U/L; reference range: 23-212 U/L) and mild hypokalemia (3.6 mEq/L; reference: 3.8-5 mEq/L). C-reactive protein (8.3 ng/mL; reference: 0.1-1 ng/mL) levels was markedly elevated.

Cervical radiography and ultrasound confirmed bilateral cervical masses, which were identified as enlarged medial retropharyngeal LNs, with the right and left LNs measuring 48.9 × 32.3 mm (Figure 2A) and 22.5 × 8.4 mm, respectively. The right mandibular LN was also enlarged (24.2 × 13.5 mm) and it showed a heterogeneous internal echotexture with peripheral blood flow signals, accompanied by a notable perinodal edema. The salivary and thyroid glands appeared normal. Abdominal ultrasonography revealed a hypoechoic nodule at the splenic head (Figure 2C), and other abdominal organs and LNs did not exhibit abnormalities. Fine-needle aspiration (FNA) and cytological examination of the enlarged LNs, including the bilateral medial retropharyngeal and right mandibular LNs (Figure 2) revealed epithelial cells with malignant features, such as anisokaryosis, multinucleation, and coarse chromatin. Similarly, splenic nodule FNA identified malignant epithelial cells that were consistent with those observed in the LNs. These findings suggested that the LNs and splenic nodule were likely secondary metastases from an unidentified epithelial tumor.

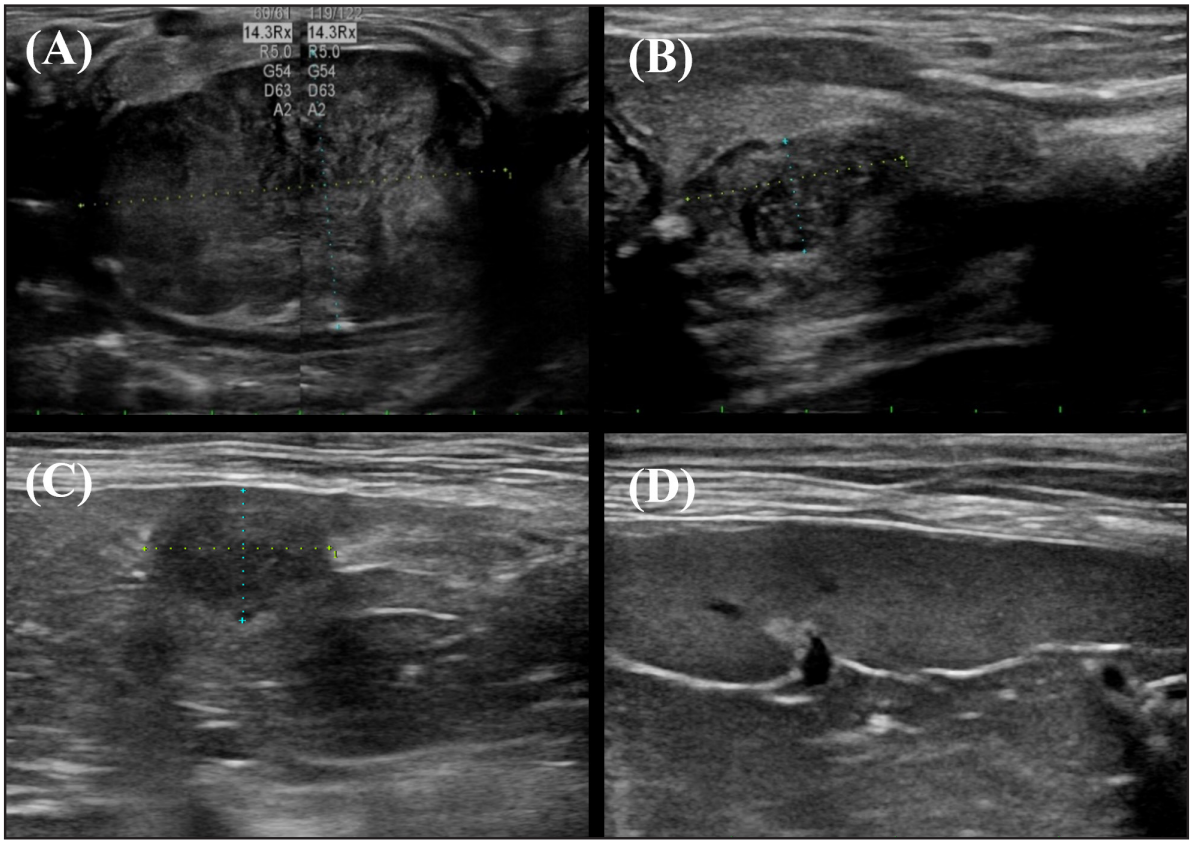

Figure 2. A & C- Ultrasound examination of the dog at initial presentation. B & D- Ultrasound after the 3rd chemotherapy cycle. A & B- Following chemotherapy, the right retropharyngeal lymph node decreased markedly in size, with resolution of perinodal edema (48 × 32 mm → 13 × 6 mm). C & D- After chemotherapy, the splenic nodule resolved, and the splenic parenchyma appeared normal.

Computed tomography (CT) imaging revealed an 11 × 9 × 15 mm soft tissue mass protruding into the oropharynx from the right palatine tonsil (Figure 4). Upon contrast administration, the mass exhibited a mild and uneven enhancement. The right medial retropharyngeal LN was significantly enlarged (40 × 32 × 50 mm) and showed a heterogeneous internal structure, rim enhancement, and calcification within the nodes. The left medial retropharyngeal and right submandibular LN were also enlarged. Evidence of tumor invasion included

a periosteal reaction at the transverse process of the C1 near the right retropharyngeal region, and thickening of adjacent muscles, including sternocephalicus and cleidocephalicus muscles, with a heterogeneous contrast enhancement. In the spleen, a hypoechoic, outward-protruding nodule with low contrast enhancement was identified. The CT findings identified a tonsillar mass, which was suspected to be the primary tumor.

Based on imaging findings and the cytological identification of malignant epithelial cells in the LNs and splenic nodule tonsillar SCC with LNs and spleen metastasis was diagnosed. At the owner's request, further confirmation via cytological or histopathological tonsillar mass examination was not performed. Treatment was then initiated and the response was closely monitored.

Carboplatin[1] was administered every 3 weeks at doses ranging from 179.4 - 207 mg/m^2, for 7 cycles. Piroxicam[2] was administered at 0.3 mg/kg once a day, with a gastrointestinal protectant and appetite stimulant. The response to chemotherapy was monitored by evaluating clinical symptoms and changes in the target metastatic lesions, including the LNs and splenic nodules. Two weeks after the 1st cycle, the dog exhibited marked appetite and vitality improvement, and the resolution of the gagging symptoms caused by the LNs' mass effect. After the 3rd cycle, its body condition score improved from 2/9 to 4/9. Using cervical ultrasonography, LN sizes were determined by summing the short axis diameters of target LNs, including the bilateral medial retropharyngeal and right submandibular LNs, following the Veterinary Cooperative Oncology Group (VCOG) consensus guidelines [18]. The sum of the short axis diameters decreased by 33% after the 1st chemotherapy cycle, indicating partial response (PR). Although the sum of the target LNs was reduced by 49% before the 4th cycle, indicating maintained PR, the left retropharyngeal LN's size increased by 80% when compared with its baseline measurement. FNA of the left retropharyngeal LN revealed predominantly pyogranulomatous inflammation, without evidence of neoplastic epithelial cells, indicating a reactive change secondary to the tumor, although the possibility of inaccurate FNA could not be ruled out. After the 3rd cycle, ultrasonography revealed decreased regional LN sizes (Figure 2B) and that the splenic nodule had disappeared, leaving a normal parenchyma (Figure 2D).

A 2nd CT scan was conducted for a more accurate chemotherapeutic effect evaluation. After the 4th chemotherapy, the post-CT evaluation revealed no significant changes and invasion of the primary tonsillar tumor when compared with before chemotherapy. However, the regional LNs, particularly the largest right retropharyngeal LN, showed a significant size reduction. Additionally, the right retropharyngeal LN's perinodal region, which exhibited signs of muscle invasion before chemotherapy, also showed improvement. The left retropharyngeal LN, which was assessed as reactive change after FNA, showed a noticeable size increment, accompanied by a fat stranding sign. Chemotherapy dosage was then increased and the response was closely monitored. Before the 7th cycle, the right mandibular LN's size was increased and the right prescapular LN, a previously unconfirmed lesion was enlarged. Because of the new lesion, the VCOG evaluation criteria changed from PR to progressive disease (PD), with the sum of the short axis diameters increasing by 47% from the nadir (Figure 5).

After the 7th carboplatin cycle, the dog had VCOG grade 4 neutropenia (neutrophil count: 0.19 × 10^9/L). The gastrointestinal symptoms were mild, with the transient grade 1 anorexia resolving spontaneously. Although the dog exhibited significant clinical improvement and notably reduced metastatic lesions, chemotherapy was discontinued and hospice care was initiated at the owner's request because of diminishing chemotherapy efficacy and VCOG grade 4 adverse effects. The dog passed away at home 53 days after transitioning to hospice care, and it survived for 208 days after diagnosis.

DISCUSSION

This case report describes the treatment of a dog diagnosed with tonsillar SCC that metastasized to the regional LNs and spleen. Primary tonsillar neoplasia is rare, and in dogs, SCCs are the most common type of tonsillar mass. A retrospective study found that of 492 dogs with tonsillar tumors, 51% had SCC. [10] Because tonsillar SCC in caudal locations from the mouth exhibits a high propensity for metastasis, tonsillar SCC is associated with poor prognosis because of its high metastasis rate and aggressiveness when compared with oral SCCs at other sites [12,17]. A retrospective study involving 123 cases found that 82% of the cases presented with regional LN metastasis, while distant metastasis, e.g., to the lungs and liver, occurred in 15% of the cases. However, metastasis to the spleen, which was observed in this case, is rare and has been previously reported in one case [15].

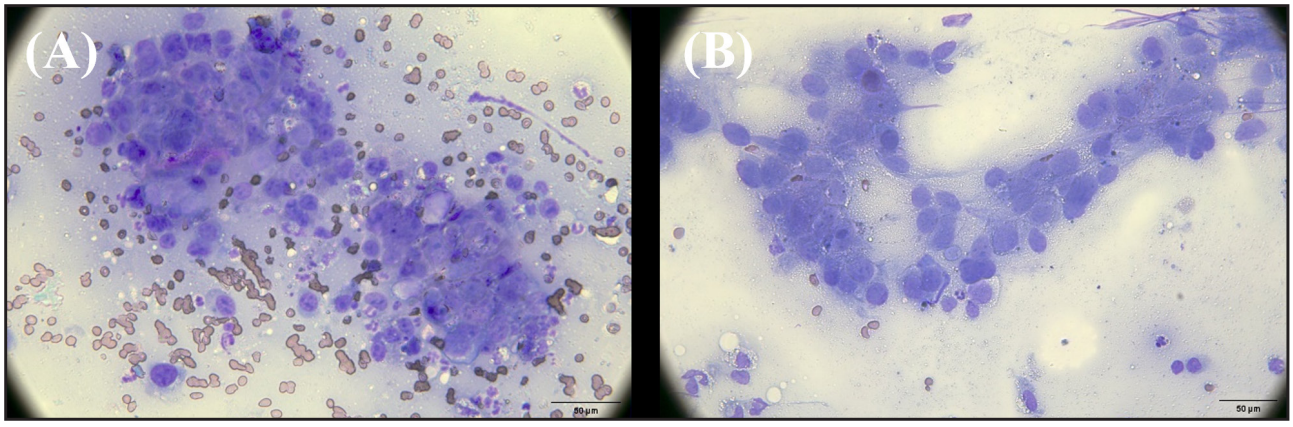

Figure 3. Cytological findings after fine-needle aspiration (FNA) of the lesions. A- Cytological analysis of the right medial retropharyngeal lymph node revealed epithelial cells with malignant features, including anisokaryosis, multinucleation, and coarse chromatin [magnification: 400x]. B- Cytological analysis of the hypoechoic splenic nodule demonstrated malignant epithelial cells, consistent with those found in the lymph nodes, suggestive of metastatic involvement [magnification: 400x].

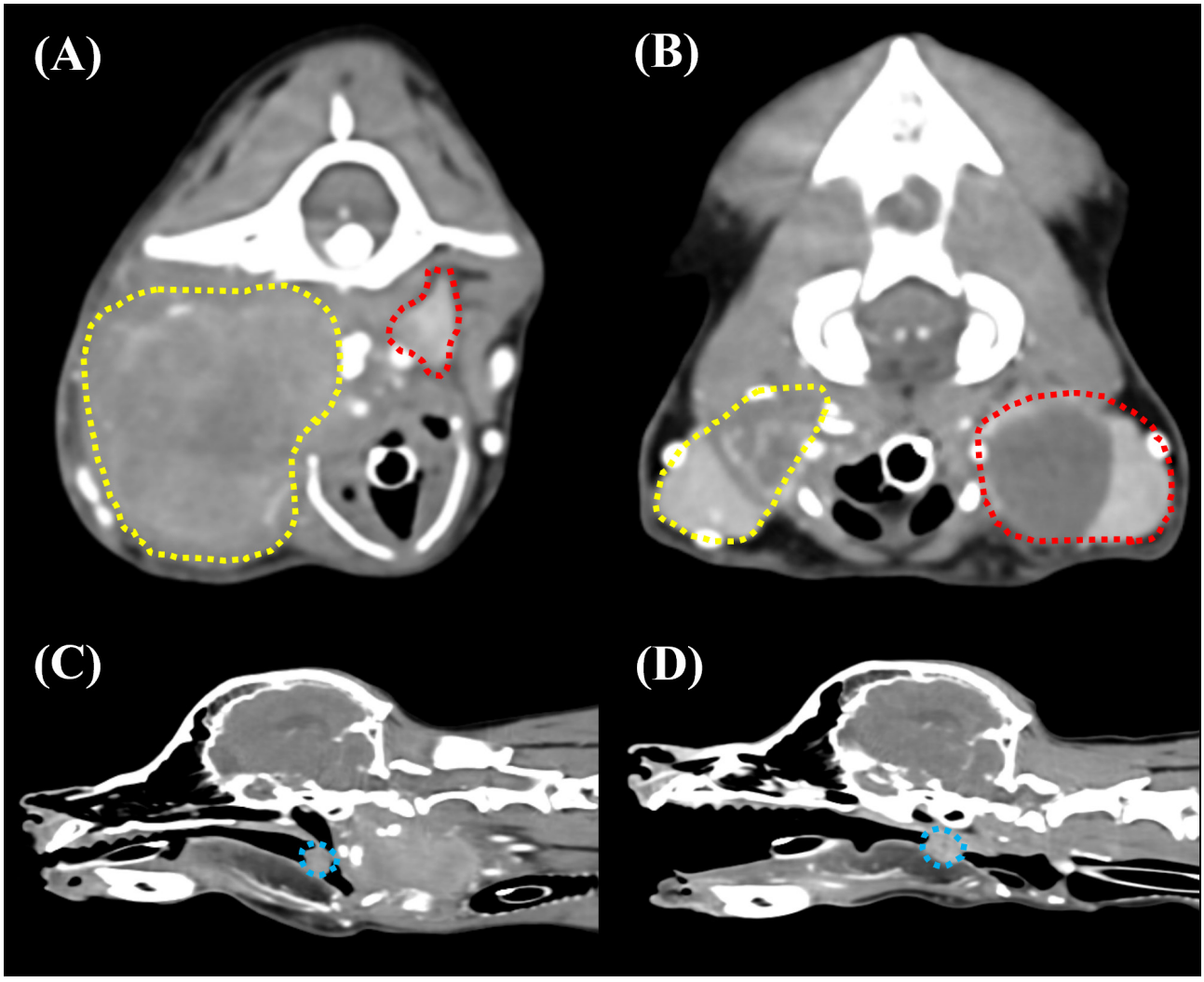

Figure 4. Computed tomography (CT) images of the dog. A & C- At initial presentation. B & D- After the fourth chemotherapy cycle. A & B- Post-chemotherapy, imaging showed a marked reduction in the size of the right retropharyngeal lymph node, with improvement in associated muscle invasion (yellow line). In contrast, the left retropharyngeal lymph node, previously considered reactive change after FNA, demonstrated interval enlargement with fat stranding (red line). C & D- No significant change was observed in the size or local invasion of the primary tonsillar mass (blue line).

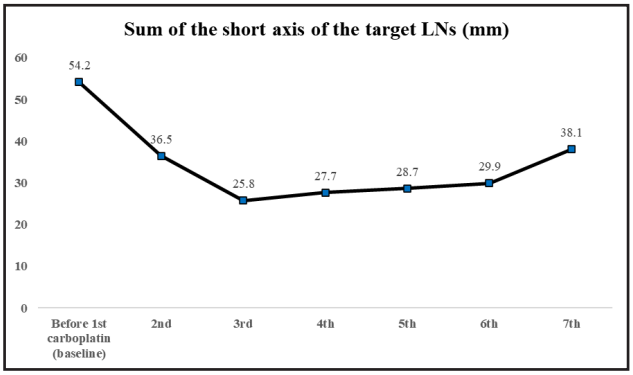

Figure 5. Response evaluation based on the sum of the short axes of target lymph nodes, including the bilateral medial retropharyngeal and right submandibular lymph nodes, as measured by ultrasonography. Baseline measurements were obtained before the 1st carboplatin administration. A partial response was observed until the sixth chemotherapy cycle, after which progressive disease was detected.

Diagnosing tonsillar tumors is challenging because the primary tumor is often small and difficult to detect through physical examination, radiography, or ultrasonography. Because of nonspecific clinical signs, tonsillar tumors are frequently identified incidentally in patients presenting with cervical lymphadenopathy [7,9]. Therefore, CT imaging is a valuable tool for tonsillar mass detection and evaluation of invasion extent, regional LN metastasis, and distant metastasis. A previous study involving 14 dogs with tonsillar tumors found that tumor-affected tonsils were generally larger than unaffected ones. However, in 3 cases, the tonsils appeared normal in size or were minimally enlarged, highlighting the potential for missed diagnoses in smaller lesions [14]. Among cervical LNs, medial retropharyngeal LN enlargement was observed in 86% of the cases, indicating it is affected more commonly than mandibular LNs [14]. Retropharyngeal LNs are suggested to be anatomically closer to pharyngeal structures and to be connected via a dense network of lymphatic and blood vessels [3]. In this case as well, medial retropharyngeal LN enlargement was primarily observed.

Tonsillar SCC treatment options include surgery, chemotherapy, radiation therapy, and NSAIDs. However, none of these has been proven as the most effective treatment. In cases without evidence of metastasis or invasion, tonsillectomy may be considered for primary tonsillar SCC, and if LNs metastasis is present, it can include regional lymphadenectomy [9,15]. In a study involving 123 dogs with tonsillar SCC, dogs that underwent surgery had a median survival time (MST) of 196 days, compared with 88 days in those that did not, indicating a survival benefit. [15] However, complete resection may be challenging because of the tumor's invasiveness. In such cases, palliative surgery may be an option. Although more radical surgical resection could potentially improve survival time, it carries a higher risk of complications, with bleeding being the most significant. [9,16]

Radiotherapy is a promising tonsillar tumor treatment option, and several studies have reported that it improves tonsillar SCC outcomes, although they are limited by small sample sizes [2,8,11,19]. Studies on radiotherapy's efficacy have reported mixed results, with some demonstrating a survival benefit and others not [7,15]. A recent study found that radiotherapy did not offer a significant survival advantage, probably because of this tumor type's inherent high recurrence and metastasis rates [7]. Further studies are needed to clarify the efficacy of radiotherapy in tonsillar SCC management.

Various antineoplastic agents have been used for tonsillar SCC, including platinum compounds (carboplatin and cisplatin), tyrosine kinase inhibitors (toceranib phosphate and imatinib mesylate), metronomic chemotherapy with cyclophosphamide, and anthracyclines (doxorubicin and mitoxantrone) [7,9,11,15]. Among these, carboplatin, which has been frequently used to treat human head and neck cancers, including tonsillar SCC, is a promising and commonly utilized chemotherapeutic agent for canine tonsillar SCC, particularly in combination with multimodal treatment protocols for enhanced therapeutic outcomes [7,11]. However, research on the most effective chemotherapy is insufficient. A retrospective study compared the response rates of 40 dogs treated with carboplatin and 30 dogs treated with toceranib and found no significant differences between the groups, with carboplatin achieving a PR of 8%, stable disease of 21%, and a PD of 31%, while toceranib achieved a PR of 9%, stable disease of 21%, and a PD of 27%. Moreover, none of the chemotherapy agents demonstrated a clear MST advantage compared to others [15]. Differences were noted between treatment groups, with the dogs receiving chemotherapy as adjuvant therapy after surgery or radiotherapy having an MST of 207 days, which indicated a survival advantage when compared with the non-chemotherapy group (MST: 109 days). In contrast, chemotherapy alone did not offer a significant MST

benefit when compared with the non-chemotherapy group [15]. Similarly, in previous studies, when used as part of a multimodal treatment approach combining surgery and radiotherapy, carboplatin demonstrated a survival benefit, while the efficacy of chemotherapy alone remained limited [7,9,11,15].

However, in this case, carboplatin alone (without surgery or radiotherapy) significantly reduced metastatic LN sizes, resolved splenic nodules, and markedly improved clinical signs, indicating PR, although the primary tumor size was not reduced. For canine malignant tumors, adjunctive NSAID therapy has been associated with a significantly longer survival, probably due to their role as COX-2 inhibitors. COX-2 is reported to be expressed in various types of dog carcinomas, including oral carcinomas, which express COX-2 receptors [4,6]. However, further studies are required to determine COX-2 expression in tonsillar carcinomas. In previous studies, the administration of NSAIDs alone or in combination with other treatments was consistently associated with a survival benefit [9,13,15]. In this case, continuous piroxicam administration without adverse effects led to an improved quality of life and suggested that as an adjunctive therapy with chemotherapy alone, NSAIDs contributed to an improved prognosis. However, because NSAIDs were administered in combination with chemotherapy in this case, their independent therapeutic effect could not be determined conclusively.

This case demonstrated notable clinical improvement and a reduction in metastatic masses following treatment with carboplatin and continuous piroxicam therapy. These findings highlight the potential efficacy of carboplatin in combination with piroxicam as an adjunctive treatment for advanced canine tonsillar SCC. While additional studies are required to determine the most effective treatment strategy, this therapeutic approach may contribute to tumor control and improved survival outcomes in affected dogs.

MANUFACTURERS

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***Declaration of interest*.** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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