

THYROIDECTOMY ASSOCIATED WITH CHEMOTHERAPY IN A DOG PRESENTING CARCINOMA IN THE THYROID GLAND

(Tireoidectomia associada à quimioterapia em cão com carcinoma na glândula tireóide)

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ABSTRACT

This study aimed to describe a case of compact thyroid carcinoma in a dog, emphasizing the diagnosis, treatment, and clinical evolution. An 11-year-old mixed-breed male canine was attended at a private clinic, complaining of swelling in the ventral cervical region and difficulty breathing. A mass close to the thyroid gland was observed in the cervical ultrasound and a mixed tumor was identified by cytology. Based on follow-up exams, the therapeutic approach to be adopted was determined: total surgical resection of the right portion of the thyroid gland, together with the parathyroid glands, followed by chemotherapy with doxorubicin. The histopathology of the tissue removed confirmed the compact thyroid carcinoma. After thyroid removal, signs of hypothyroidism were confirmed by the hormonal dosage and the canine received hormone replacement with Levothyroxine as treatment, ceasing the symptoms. During routine follow-up, the presence of miliary pulmonary metastases was identified. The patient continued with the chemotherapy sessions, presenting a stable condition for almost 6 months after starting the treatment. However, clinical signs of dyspnea were manifested, resulting in a gradual worsening. Thus, the tutors chose to euthanize the animal after 9 months of treatment. According to the case described, thyroidectomy is an option of treatment for cases of thyroid carcinoma with wide dimensions. However, the technique's success depends on the effective and complete removal of the affected tissue due to the high frequency of metastases and the possible occurrence of secondary hypothyroidism.

Keywords: Cancer, hypothyroidism, canine, thyroid removal.

RESUMO

Objetivou-se, neste trabalho, descrever um caso de carcinoma compacto de tireoide em cão, enfatizando o diagnóstico, o tratamento e a evolução clínica. O paciente foi atendido em uma clínica particular, sendo um canino macho, sem raça definida, de 11 anos, com queixa de edema cervical ventral e dificuldade respiratória. Pela ultrassonografia cervical, foi observada uma massa próxima à glândula tireoide e pela citologia, um tumor misto. A partir dos exames de acompanhamento, foi determinada a conduta terapêutica a ser adotada: ressecção cirúrgica total da porção direita da glândula tireoide, junto às paratireóides, seguida de quimioterapia com doxorubicina. A histopatologia do tecido removido confirmou o carcinoma compacto da tireoide. Após a remoção da tireoide, sinais de hipotireoidismo foram confirmados pela dosagem hormonal, sendo feita reposição hormonal com Levotiroxina, cessando os sintomas. Durante o acompanhamento de rotina, foi identificada a presença de metástase pulmonar miliar. O paciente continuou suas sessões de quimioterapia, mantendo um quadro estável por quase seis meses após o início do tratamento. No entanto, sinais clínicos de dispnéia foram manifestados, com piora gradativa do quadro, tendo os tutores optado pela eutanásia do animal após nove meses do início do tratamento. De acordo com o exposto, conclui-se que a tireoidectomia é um tratamento de escolha para os casos de carcinoma de tireoide com amplas dimensões. Entretanto, o sucesso da técnica depende da remoção efetiva e completa do tecido afetado, devido à alta frequência de metástases, além de poder ser acompanhada por um quadro de hipotireoidismo secundário.

Palavras-chave: Neoplasia, hipotireoidismo, canino, remoção da tireoide.

INTRODUCTION

Oncology represents a great and important specialty of Veterinary Medicine. The increase in the life expectancy of pets, especially dogs and cats, is directly related to the increase in the incidence of neoplastic cases and to the greater emphasis given to the veterinary oncology area (ROSSETTO *et al.*, 2009).

Tumors in the thyroid are relatively common, with an incidence ranging from one to three percent of dogs with neoplasia (LIPTAK, 2007). The thyroid is a small, elongated gland, fixed on the outer surface of the proximal trachea portion (DALECK and DENARD, 2016). Although surgery to excise the thyroid is one of the possible treatments (LIPTAK, 2007), a thyroidectomy is a possible cause of hypothyroidism (MONTANHA and LOPES, 2011), which triggers a multisystemic disease, manifested by impaired production of its hormones, essential to maintaining organic homeostasis (NELSON and COURO, 2010). Nevertheless, the permanence of this condition is rare after the removal of the gland, which is due to the presence of accessory thyroid tissue (CATHARINE *et al.*, 2004).

Usually, thyroid neoplasia in dogs is classified into adenomas and carcinomas, considered benign and malignant tumors, respectively (ROSOL and MEUTEN, 2016). The latter are more frequent (60 to 90%) (KENT *et al.*, 2002), and are distinguished from the first by the manifestation of capsular and vascular invasion (ROSOL and MEUTEN, 2016). Thus, biopsy or histopathological examination provides the definitive diagnosis (LIPTAK, 2007), and is a decisive point for treatment and therapy, which vary according to the size of the tumor, invasion into adjacent structures, and the presence of metastases (BARBER, 2007).

Based on the above, the objective of this report was to describe a case of compact thyroid carcinoma in a dog, with an emphasis on diagnosis, treatment, and clinical evolution.

PATIENT SERVICE

An 11-year-old male canine, without defined breed, was attended at a Veterinary Oncology Clinic, located in Recife city. The animal was referred by another veterinarian, who had attended the dog with the complaint of increased volume in the ventral region of the neck. During the consultation, it was possible to observe that the animal had dyspnea, however it presented normophagy, normodipsy, normoqueia, and normuria, with no other clinical complaint. In addition, through cervical ultrasound, a nodule close to the thyroid was identified and the cytology identified it as a mixed tumor.

In order to monitor the patient's condition and plan the best therapeutic approach, the following exams were requested: chest radiography for metastasis research, ultrasonography (USG) of the abdominal cavity to assess organs and search for metastases, blood count and biochemicals, urea and creatinine, and alanine aminotransferase (ALT) and alkaline phosphatase (FA), to assess kidney and liver function, respectively. Through the radiography, signs indicating pulmonary senescence and preserved cardiac silhouette were observed, with no signs of cardiogenic pulmonary edema and no evidence of primary or metastatic neoplasia (Fig. 01). In turn, only splenomegaly was observed by means of cavitory USG, without the presence of metastatic lesions in parenchymal abdominal organs at the time of the examination (Fig. 02).



Figure 01: Initial radiographic images of the chest, obtained for metastasis investigation in canine patient with suspected thyroid neoplasia, with verification only of pulmonary senescence.

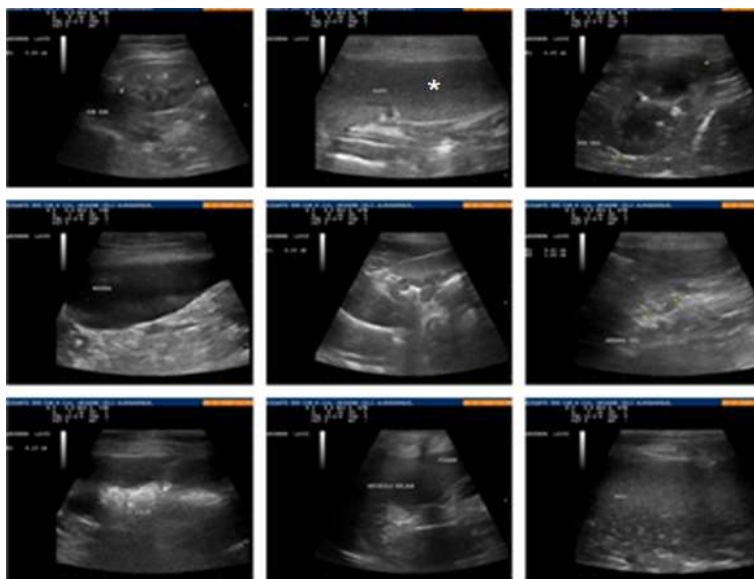


Figure 02: Cavity ultrasonography performed on a canine patient with suspected of thyroid neoplasia, eliminating the presence of metastasis and demonstrating splenomegaly (*).

Computed tomography (CT) is always requested in the clinic's routine for surgical planning, since it makes it possible to delimit the extension of the affected area, the invasion of adjacent tissues and, mainly, the viability of the surgery. In the case in question, the evaluation of the cervical region indicated the presence of a large mass (5.39cm x 2.52cm), in the ventral portion of the investigated area, which started at the level of the Hyoid bone, lateralized to the right, and extended to the C3 vertebra. Moreover, compression caused by the tumor in the trachea was visualized, with consequent tracheal collapse. Despite the involvement of the right thyroid lobe, the left lobe was compatible with normal thyroid tissue, and the retropharyngeal lymph nodes did not show signs of metastatic invasion at the time of the examination (Fig. 03).

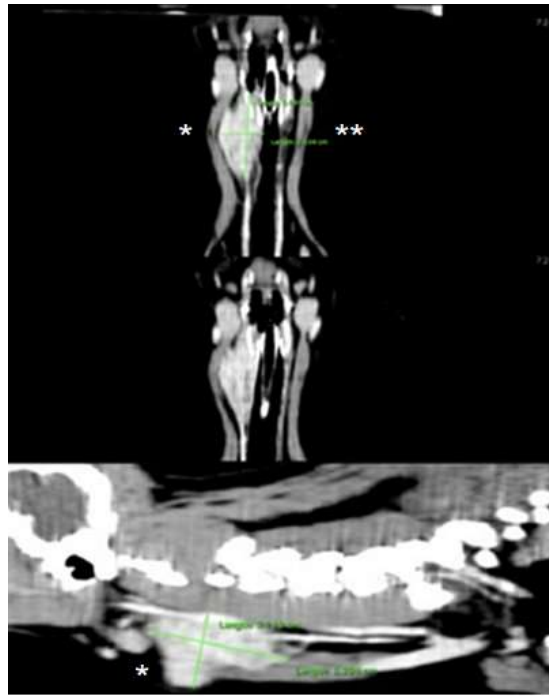


Figure 03: Computed tomography images of the cervical region. Thyroid neoplasia in canine (*). Volume increase ventrally and lateralized to the right, without left involvement (**).

Based on the results of normal hematological and biochemical tests, as well as radiography, USG, tomography, and surgical risk, it was verified that the animal was able to undergo surgical resection of the thyroid nodule. The decision for the total thyroidectomy of the right lobe of the thyroid gland, in association with chemotherapy, was taken together with the owner.

To prepare the patient in relation to the thyroidectomy procedure, venous access was performed, with administration of pre-anesthetic medications and the trichotomy in the surgery area. The animal was then conducted to the operating room and intubated and placed in the supine position on the operating table, ready for the surgical procedure (Fig. 04).



Figure 04: Canine, male, SRD properly prepared to perform the surgical procedure for the removal of the right thyroid lobe affected by carcinoma, positioned on the surgery table.

The duration of the surgery was approximately two hours. Initially, there was excessive bleeding that was controlled after ligation of the vessel that irrigated the neoplasia, and for this reason it was necessary to perform a blood transfusion during the trans-operative period. The tumor proved to be quite adherent to the structures adjacent to it, which made the divulsion difficult. Thus, in addition to the right thyroid and parathyroid, part of the sternohyoid and cephalic sternum muscles needed to be removed and sent for histopathological study, due to the manifestation of changes in their organizations (Fig. 05).

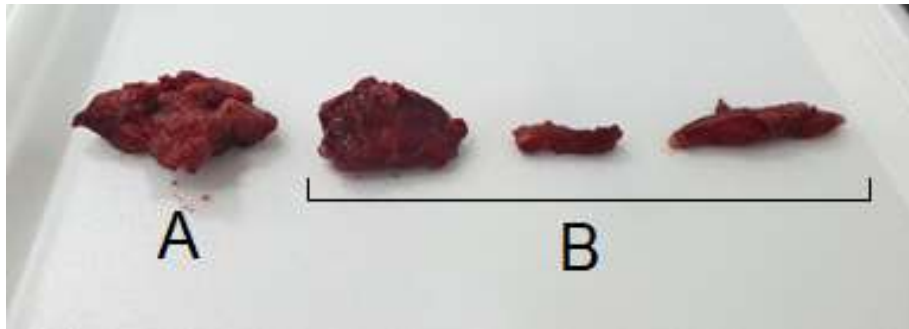


Figure 05: Anatomical structures of canine, male, SRD affected by carcinoma and surgically removed and destined for histopathological analysis.

Obs.: Right thyroid lobe and parathyroid (A) and fragments of skeletal muscle (B).

The tissue fragments removed surgically were fixed in 10% buffered formaldehyde and stored in appropriate containers for later histopathological analysis. The histopathological result showed that the tumor was a compact (solid) carcinoma for the thyroid and a metastatic thyroid carcinoma for the muscle fragments. The surgical margins of the fragments were compromised, as well as the vascular margins, indicating that the tumor tissue was not completely removed.

As part of the treatment protocol, chemotherapy with the drug Doxorubicin was instituted 13 days after the surgical intervention, at a dose of 1mg/kg, intravenously, at intervals of 21 to 30 days, totaling 4 sessions. The first chemotherapy session occurred with the administration of Emedron and Promethazine, at doses of 0.4mg/kg and 1mL/20kg, respectively, before chemotherapy, as prophylaxis to nausea and allergic reactions, respectively. Prior to each session, hematological examinations and echocardiography were recommended, in order to investigate possible changes arising from the toxic action of the medication, mainly in cardiomyocytes. However, the patient did not experience adverse reactions during the therapy. He remained relaxed and even slept due to the sleepiness caused by the pre-chemotherapy medications.

Parallel to the cancer treatment, the patient was referred to a veterinarian endocrinologist, in order to ascertain the endocrinological status after the loss of one thyroid lobe, considering the risk of developing hypothyroidism. Tests of dosage for total T4, free T4, and canine TSH hormones were ordered by the doctor. The results showed that the patient had developed hypothyroidism, since the T4 levels were low, while the TSH level was above the reference values (Tab. 01).

Table 01: Hormone levels of the canine, male, SRD 2 months after the right thyroidectomy.

Hormone	Serum dosage	Reference value
Thyroxine (T4)	0.36	1.25-3.90µg/dL
Free thyroxine (T4 F)	0.25	0.82-3.65ng/dL
Canine TSH	2.98	0.10-0.60ng/dL

TSH: thyroid stimulating hormone.

The owner reported that the animal manifested exercise intolerance, tiredness, apathy, cold skin, and panting. In view of this, hormone replacement was initiated with the use of Tyrox 200mcg (Levothyroxine sodium), at a dose of 0.02mg/kg every 12 hours. However, after 3 weeks of use, the dog showed no improvement, and the dose of the drug was increased to 0.04mg/kg every 12 hours. After this readjustment, a clinical improvement was clearly perceived.

In addition to the implementation of hypothyroidism treatment, new imaging tests were requested two months after the thyroidectomy surgery, chest radiography for metastasis research and abdominal ultrasonography, to monitor the patient's condition. On the chest radiography, the pulmonary pattern was suggestive of miliary alteration with the impression of multiple small nodules, that is, the presence of miliary pulmonary metastasis (Fig. 06). In turn, the abdominal ultrasonography showed no changes.



Figure 06: Canine chest X-ray images 2 months after thyroidectomy and chemotherapy, where signs of miliary pulmonary metastases are evident.

Despite the aforementioned results, chemotherapy sessions proceeded normally. To date, the canine has undergone four chemotherapy sessions with the drug Doxorubicin and with the use of cyclophosphamide. The animal presented active and without any clinical complaints. Moreover, the tumor removal area did not change, indicating that there were no recurrences at the site.

RESULTS AND DISCUSSION

Most dogs with thyroid carcinoma, which corresponds to approximately 60%, are taken to veterinary clinics due to the presence of masses in the cervical region (LEAV *et al.*, 1976). Thyroid tumors are most commonly reported in older dogs and medium-sized to large-breeds (HARARI *et al.*, 1986; WUCHERER and WILKE, 2010), in particular, the Siberian Husky, Golden Retriever, and Beagle show a more significant risk of developing thyroid neoplasia (LISA, 2007; WUCHERER and WILKER, 2010). The mean age of onset of clinical signs with a thyroid tumor is 10 years, with no sexual predilection (NELSON and COUTO, 2010).

The above information was confirmed by the clinical case described, where the older animal involved had a large nodule in the right lobe of the thyroid, which pressed on his trachea and thus caused respiratory distress. In contrast, the left portion of the gland retained its structure and normal tissue aspect, a finding that corroborates the evidence that the unilateral involvement of the gland, in cases of thyroid carcinoma, is approximately twice as frequent as the total involvement (CAPEN, 2002).

The choice of treatment for thyroid tumors depends on the variables being analyzed, such as the type and size of the tumor, extent of invasion, and therapeutic availability, in addition to the presence of metastasis (LUNN and PAGE, 2013, LISA and BARBER, 2007). Radiation therapy is indicated for dogs with fixed and invasive thyroid carcinomas (LIPTAK, 2007). The surgery for the thyroid gland excision, in cases of tumors, is the most recommended treatment (CARVER *et al.*, 1995; FREDERICK *et al.*, 2020). Therefore, these and other factors must be considered in order to make the most sensible decision in relation to each clinical case.

For the dog in question, the inexistence of a radiotherapy device limited the treatment options. Among those raised were the surgical procedure or the use of chemotherapy drugs, combined or isolated. Because the chest X-ray did not show pulmonary metastasis, in association with the results of other tests indicative of surgical risk, the decision was to perform the right thyroidectomy combined with chemotherapy. The use of chemotherapy should be recommended after surgery or radiation therapy in dogs at a high risk of developing metastases (THEON *et al.*, 2000). However, the continuation of the treatment should consider the risks and benefits, and the characteristics of the tumor, such as type after the biopsy result (LIPTAK, 2007).

Although radiotherapy is the most recommended treatment for fixed and invasive thyroid carcinomas (LEAV *et al.*, 1976), this is not a reality in northeastern Brazil, as it is currently carried out only in the Southeast. For this reason, the chemotherapy protocol with Doxorubicin was used, which has been shown to be active against thyroid carcinoma in dogs (JEGlum and WHEREAT, 1983). It is worth noting that chemotherapy with the drugs Doxorubicin or Cisplatin should be recommended after surgery or radiotherapy, due to the risk of developing metastases (CARVER *et al.*, 1995; TOCHETT *et al.*, 2017).

According to FREDERICK *et al.* (2020), metastatic disease in dogs with thyroid tumor is not very common, with an incidence of around 4%. Moreover, previous results show that the risk of metastatic disease is greater in bilateral thyroid tumors (HARARI *et al.*, 1986; THEON *et al.*, 2000). However, as this case describes an invasive carcinoma with indefinite limits, complete removal of the altered tissue was not possible. This was confirmed by the

histopathology, through which it was found that the margins of the extracted tissues were compromised, a fact that may have contributed to the subsequent development of miliary pulmonary metastasis, confirmed through the new imaging exams performed to monitor the patient.

Additionally, it is described in the literature that canine patients who undergo thyroid excision, usually do not show clinical signs of thyroid dysfunction (LISA and BARBER, 2007). In contrast, in the case reported, it was observed that the thyroidectomized dog clinically manifested hypothyroidism, corroborating with Nadeau and Kitchell (2011), Radlinsky (2007) and Worth *et al.* (2020), who reported that hypothyroidism is one of the possible complications after thyroidectomy. This can be associated with the occurrence of laryngeal paralysis (PANCIE, 2021), an important complication resulting from thyroidectomy (REAGAN *et al.*, 2019).

Based on the above, the detailed follow-up of the animal with thyroid carcinoma, even after surgery and chemotherapy, is crucial for the identification of complications and metastases. In this way, it is possible to contribute to the stabilization of the condition and better quality of life for the patient.

CONCLUSION

Thyroidectomy is a treatment of choice for cases of thyroid carcinoma with wide dimensions. However, the success of the technique depends on the effective and complete removal of the affected tissue, since it is a tumor type with a high frequency of metastases. In addition, hypothyroidism secondary to thyroidectomy is a possible reality, which results in the need for specialized medical follow-up.

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