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Histopathology, epidemiology and post-operative survival of canine thyroid carcinoma

Daiane Cristine Lopes Duarte
São Paulo State University (UNESP)
Faviana Aimé Maza León
f.leon@unesp.br

São Paulo State University (UNESP)
César Passareli Candido Lobo
São Paulo State University (UNESP)
Fábio Sossai Possebon
São Paulo State University (UNESP)
John Patrick Kastelic
University of Calgary
Alessandre Hataka
São Paulo State University (UNESP)

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Abstract

Thyroid tumors, the most common neuroendocrine neoplasms in dogs, account for approximately 1–4% of all canine tumors. The objective was to evaluate histopathology, epidemiology and postoperative survival of canine thyroid carcinoma. Data were obtained from the Pathology Service at the Sao Paulo State University. Histopathological evaluation was performed, and breed, sex, and age were analyzed. Eleven cases were included, with compact-follicular carcinoma being the most frequently diagnosed subtype. The mean age at diagnosis was 8.9 years (median age, 10 years), with no significant differences regarding sex or breed distribution. Median and longest survival times were 333.7 and 1050 days, respectively. These findings contribute to characterizing canine thyroid carcinoma in a referral population.

Introduction

Thyroid cancer is the most common endocrine neoplasm in dogs, representing approximately 1–4% of all canine tumors (Tsimbas et al., 2019; Hassan et al., 2020). It primarily affects older animals (mean, 9–10 years), with Beagles, Boxers and Golden Retrievers being overrepresented. Unilateral lobe involvement is more frequent than bilateral. Approximately 50–60% of affected dogs are euthyroid, 30–40% are hypothyroid, and 10–20% are hyperthyroid (Jankovic et al., 2021; Enache et al., 2023). The most common clinical sign tumor is a ventral cervical mass. Coughing, tachypnea, dyspnea, dysphagia, and dysphonia can also occur (Frederick et al., 2020), due to tracheal compression or pulmonary metastases (Harari et al., 1986).

The etiology of thyroid tumors in domestic animals is unclear. In dogs, hypothyroidism and chronic lymphocytic thyroiditis are potential risk factors (Barber, 2007). In humans, exposure to ionizing radiation in the cervical region is a well-established predisposing factor, and environmental influences, e.g., dietary iodine intake, are also implicated.

A potential genetic component of canine thyroid carcinoma was investigated in Beagles. In one study, hypothyroidism secondary to spontaneous lymphocytic thyroiditis significantly increased the incidence of thyroid tumors, which were both more frequent and had higher malignancy grades in hypothyroid versus euthyroid dogs. In addition to a potential hereditary predisposition, this also implicates chronic TSH stimulation underlying neoplastic progression, as none of the affected dogs received thyroid hormone replacement therapy. TSH may induce angiogenesis by upregulating VEGF (Verschueren et al., 1992; Soh et al., 1996).

Histological diagnosis of thyroid tumors is most commonly done after thyroidectomy. However, 50–75% of these tumors are unresectable due to invasive growth. An incisional or needle biopsy may be required. Cytology can facilitate differentiation between neuroendocrine and thyroid origins of the tumor. However, a Tru-Cut biopsy is generally discouraged due to the risk of severe hemorrhage (Townsend & Ham, 2022).

Thyroid tumors can originate from epithelial or mesenchymal tissues (Cook et al., 2022). Most canine thyroid neoplasms (60–90%) are carcinomas, arising from either gland-follicular cells or C-cells, resulting in Follicular Thyroid Carcinoma (FTC) or C-cell (medullary) Thyroid Carcinoma (CCTC), respectively. The World Health Organization (WHO) classifies human follicular thyroid carcinomas into well differentiated (with subtypes), poorly and undifferentiated neoplasms with subtypes like carcinosarcoma, whereas medullary thyroid carcinomas are a separate entity. Well-differentiated follicular thyroid carcinomas include follicular, mixed, compact and papillary subtypes (Campos et al., 2014; Soares et al., 2020). The WHO classification for thyroid tumors in animals' parallels that used in humans, but is less detailed and updated less frequently (Athey et al., 2024). Immunohistochemistry (IHC) is useful to determine the cellular origin of canine thyroid tumors, although most cases are diagnosed based on histomorphology (Newman et al., 2022).

The majority of thyroid tumors in dogs are malignant, and 16–60% of affected animals have evidence of metastasis at the time of diagnosis. Dogs have a higher incidence of metastatic disease than humans, as most human thyroid cancers are of the papillary subtype, with a favorable prognosis and infrequent metastasis (Hassan et al., 2020).

The objective was to evaluate histopathology, epidemiology and postoperative survival of canine thyroid carcinoma.

Material and Methods

Case Selection

Data were obtained from the Pathology Service at the Sao Paulo State University, over a 10-year period. In total, 3,317 cases were reviewed, of which 11 (0.33%) were diagnosed with thyroid carcinoma. Each record included animal age, breed and sex, date of the examination, and lesion information (location, dimensions, macroscopic description, microscopic findings, and diagnosis). Additional data regarding treatment and clinical outcomes were included when available. Cases with insufficient or missing information were excluded.

Histopathology

Tissue fragments were fixed in a 10% buffered formalin, dehydrated, cleared and embedded in paraffin blocks. Five-micrometer tissue sections were obtained, stained with Hematoxylin and Eosin (H&E), mounted on slides and cover slipped.

The histologic type of primary tumors was classified according to the WHO classification (Kiupel *et al.*, 2008) (Table 1). All tumors were reviewed by specialist pathologists, who confirmed and validated the diagnoses.

Table 1
Classification of thyroid neoplasms according to the WHO.

Source. (Kiupel *et al.*, 2008).

1. **Tumors of thyroid follicular cells**
1.1 Follicular Thyroid Adenoma
1.1.1 Microfollicular Thyroid Adenoma
1.1.2 Macrofollicular Thyroid Adenoma
1.1.3 Cystadenoma of the Thyroid
1.1.4 Papillary Thyroid Adenoma
1.1.5 Trabecular/Solid Thyroid Adenoma
1.1.6 Oxyphilic Thyroid Adenoma (“Hurthle,” Oncocytic)
1.2 Follicular Thyroid Carcinoma
1.2.1 Well-Differentiated Thyroid Carcinoma
1.2.1.1 Follicular Thyroid Carcinoma
1.2.1.2 Compact (Solid) Thyroid Carcinoma
1.2.1.3 Compact-Follicular Thyroid Carcinoma
1.2.1.4 Papillary Thyroid Carcinoma
1.2.2 Poorly Differentiated Thyroid Carcinoma
1.2.3 Undifferentiated Thyroid Carcinoma
1.2.3.1 Spindle Cell Thyroid Carcinoma
1.2.3.2 Small Cell Thyroid Carcinoma
1.2.3.3 Giant Cell Thyroid Carcinoma
1.2.4 Carcinosarcoma of the Thyroid
2. **Nodular lesions of the thyroid follicular cells**
2.1 Nodular (Multinodular) Hyperplasia of the Thyroid
2.2 Diffuse Hyperplasia of the Thyroid Follicular Cells
2.3 Ectopic (Accessory) Follicular Cells
3. **Tumors of the thyroglossal duct remnants**
3.1 Adenoma of the Thyroglossal Duct Remnant
3.2 Carcinoma of the Thyroglossal Duct Remnant
4. **Tumors of parafollicular cells (C Cells)**

4.1 Adenoma of the C Cells

4.2 Carcinoma of the C Cells

Statistical analyses

Descriptive statistics (minimum, maximum, mean, median and percentage) were calculated. Furthermore, a Chi-square test was performed to assess the statistical significance of differences between sex and breeds. Survival analysis was carried out using the Kaplan-Meier method.

AI Use

The authors declare that Artificial Intelligence (AI) tools, such as Chat GPT, were used solely to improve the clarity and language of the manuscript; all scientific ideas, analyses, and interpretations are those of authors.

Results

A total of 3,317 cases reviewed (Fig. 1), of which 11 (0.33%) were diagnosed with thyroid carcinoma. All 11 cases contained complete information and were included in the analysis. Among the affected dogs, three (27.3%) were males and eight (72.7%) were females. The distribution of breeds included three (27.3%) mixed-breed, two (18.2%) Labrador Retrievers, and one (9.1%) each of the following: Australian Cattle Dog, Cocker Spaniel, Siberian Husky, Maltese, and Miniature Pinscher (Table 2).

Table 2
Epidemiological, survival, and outcome data of dogs with thyroid neoplasm.

N	Age (years)	Breed	Sex	Survival (months)	Outcome
1	6	Labrador Retriever	F*	30	Alive
2	11	Mixed-breed	F	NP*	NP
3	13	Cocker Spaniel	F	NP	NP
4	7	Labrador Retriever	F	NP	NP
5	8	Mixed-breed	F	NP	NP
6	6	Mixed-breed	M*	28	Alive
7	10	Maltese	M	35	Alive
8	11	Miniature Pinscher	M	5	Euthanasia
9	10	Australian Cattle Dog	F	7	Euthanasia
10	11	Boxer	F	1.5	Euthanasia
11	5	Siberian Husky	F	NP	Euthanasia
* - F - female, M - male, NP - not provided.					
Source. Personal archive.					

Ages of affected dogs ranged from 5 to 13 years, with a mean of 8.9 years and a median of 10 years. The distribution of thyroid carcinoma across sex and breed was homogeneous ($p = 0.13$ and $p = 0.90$), indicating no significant differences in prevalence among these groups.

Among the 11 cases, six (54.6%) were classified as compact-follicular carcinoma; of these, three (50%) exhibited neoplastic cell emboli, whereas the remaining three (50%), did not. Three cases (27.2%) were identified as compact/solid carcinoma, with two (66.7%) presented embolism and one (33.3%) lacking this feature. The remaining two cases (18.2%) were undifferentiated giant cell carcinoma; both had neoplastic emboli in blood and/or lymphatic vessels. Histopathological findings are described in Table 3.

Table 3
Anatomopathological diagnoses of dogs with thyroid neoplasms, according to the WHO

N	Carcinoma Subtype	Vascular/lymphatic embolism
1	Compact-follicular of the thyroid	Present
2	Compact-follicular of the thyroid	Present
3	Compact-follicular of the thyroid	Absent
4	Compact-follicular of the thyroid	Absent
5	Compact-follicular of the thyroid	Absent
6	Compact-follicular of the thyroid	Present
7	Compact/solid of the thyroid	Present
8	Compact/solid of the thyroid	Absent
9	Compact/solid of the thyroid	Present
10	Undifferentiated giant cell of the thyroid	Present
11	Undifferentiated giant cell of the thyroid	Present
Source. Personal archive.		

Compact-follicular thyroid carcinomas were diagnosed when well-differentiated neoplastic follicular cells exhibited a mixed solid and follicular growth pattern in approximately equal portions. The neoplastic cells were arranged in compact nests that appeared morphologically and functionally less differentiated than normal thyroid follicles (Fig. 1).

Compact (solid) thyroid carcinomas were a well-differentiated neoplasm in which most follicular cells were arranged in compact and/or solid aggregates. Microscopically, densely packed solid cell clusters were separated by fibrous stroma, with few or poorly defined follicular structures. Colloid secretion was rare or absent. Neoplastic cells were polyhedral and tightly packed, exhibiting eosinophilic, finely granular, or occasionally vacuolated cytoplasm (Figs. 2 and 3).

In cases diagnosed as undifferentiated giant-cell thyroid carcinoma, the neoplastic population was composed of highly malignant, pleomorphic cells that were giant, small, or spindle-shaped. Atypical mitotic figures were frequent, accompanied by cellular cannibalism, bizarre nuclear forms, and prominent nucleoli. Both cases exhibited vascular and lymphatic emboli as well as evidence of distant metastasis (Fig. 4).

The longest survival time was 1050 days in a dog diagnosed with compact/solid thyroid carcinoma. Two additional dogs, both with compact-follicular carcinomas, survived for the entire observation period, with follow-up durations of 900 and 840 days, respectively. Overall survival rate at the end of the study was

42.8% (3 of 7 dogs). Among dogs that died, one had an undifferentiated giant-cell carcinoma and died 45 days after diagnosis. Two others had compact/solid carcinomas and died after 930 days. Mean survival time for these four animals was 333.7 days (Fig. 5).

Discussion

In the current study, mean age was 8.9 years, consistent with thyroid tumors usually affecting adult or aged dogs (mean age, 9 years) (Grubor & Haynes, 2005). Furthermore, male and female dogs were equally represented. In human thyroid cancer, women exhibit a higher incidence of tumors than men. This increased susceptibility is attributed to hormonal influences, a more reactive immune system, which predisposes them to autoimmune thyroid diseases and greater medical surveillance (Tran & Davies, 2023). In dogs, sex predisposition has not been demonstrated. In contrast to humans, where has been confirmed that females are more affected than males with both familial or sporadic occurrences, whereas in dogs these neoplasms are rare and a potential familial origin has not been extensively investigated (Suepaul et al., 2024).

Although previous studies have reported breed predispositions for thyroid carcinoma, particularly in Boxers, Beagles, Siberian Huskies, and Golden Retrievers (Dobson, 2013; Coelho-Vinhais et al., 2024), our findings did not align with this pattern. In the present study, mixed-breed dogs were overrepresented, and the most common pure breed affected was the Labrador Retriever, with only a single Husky and no Beagles identified. Similarly, our results contrasted with those of a Brazilian study in which 65.4% of affected dogs were of a defined breed (Tochetto et al., 2017). Among these, Boxers accounted for 15.4% of cases, other breeds with a higher incidence were Rottweilers and Fila Brasileiro, and only 34.6% of cases were mixed-breed dogs. (Tochetto et al., 2017). However, these apparent discrepancies may reflect a limited sample size, rather than true biological variation. Future studies with larger samples and population-based denominators are needed to clarify the relationship between breed, sex, and other epidemiological factors in the development of thyroid carcinoma in dogs.

In the present study, median survival time was 32 months. Although lower than previously reported, this finding remains consistent with the prognosis described in the literature for this histologic subtype. Median survival of dogs with thyroid carcinoma ranged from 1.5 months to 4.5 years (Giannasi et al., 2021). Follicular thyroid carcinoma has a median survival of 27 to 30 months under treatment, whereas untreated dogs have a median survival time of only 3 months (Jankovic et al., 2024). The median survival for dogs with solid follicular tumor that are treated with surgery alone has been reported to be as long as 44 months (Slensky et al., 2003).

In the present study, the dog diagnosed with undifferentiated giant cell carcinoma had a markedly short survival (45 days after diagnosis). In dogs, undifferentiated giant cell carcinoma is an uncommon but highly aggressive tumor arising from poorly differentiated follicular cells and lacks the characteristic architectural pattern of arrangement of tumor cells (Doneley & Suen, 2022). In humans, this tumor

subtype also has an extremely poor prognosis, reported survival rates of approximately 18% at 1 year and only 0–10% at 5 years after diagnosis (Moreno et al., 2022).

In our study, 54.6% of the tumors were classified as compact-follicular carcinoma, supporting the microscopic patterns and the prevalence in the canine population examined.

Follicular, mixed and solid subtypes are the most commonly diagnosed thyroid carcinoma in dogs. Mixed follicular carcinomas are often reported as the most prevalent and are characterized by equal portions of follicular and compact neoplastic growth, with neoplastic follicles that may be smaller and contain less colloid than observed in the follicular pattern. Few studies indicate that the solid type may be more common than other subtypes, and some have suggested this is the least differentiated subtype among the well-differentiated follicular thyroid carcinomas, whereas mixed and follicular represent intermediate and the most differentiated subtypes, respectively (Fontes et al., 2023; Athey et al., 2024; Dark et al., 2024).

In a study evaluating the prognostic value of IHC in differentiating follicular thyroid carcinoma from medullary thyroid carcinoma, medullary tumors were significantly less likely to be locally invasive at diagnosis, suggesting a higher likelihood of complete surgical excision. However, no significant differences were found between tumor types regarding metastatic disease at presentation, overall or disease-free survival, metastasis-free interval, or recurrence after thyroidectomy, indicating comparable postoperative outcomes (Campos et al., 2014).

Microvascular invasion (MVI), defined as the presence of tumor cells within blood vessels, is an important factor in cancer progression and prognosis in humans. Histologically confirmed MVI is recognized as a marker of aggressive disease, and affected patients have a higher risk of metastasis at the time of diagnosis as well as an increased likelihood of distant recurrence (Huo et al., 2025). Patients with MVI are more likely to present with metastatic disease and experience distant recurrence.

In contrast, Campos et al. (2014) reported no association between MVI and overall survival. This discrepancy may be explained by the typically indolent course of thyroid carcinoma metastases, which often progress slowly and are not necessarily accompanied by rapid clinical deterioration. In that study, the overall median time to distant metastasis was approximately twice median overall survival, supporting the notion that metastatic progression may occur long before it has a measurable impact on overall survival.

The exclusion of necropsy cases in the present study represents a limitation, as it may have led to an underestimation of the true prevalence of thyroid neoplasm. It’s possible that many thyroid neoplasms remain undiagnosed until necropsy (Hayes & Fraumeni, 1975). Several studies have reported that most thyroid adenomas are incidental findings at necropsy, as they tend to be small, freely moveable and not produce clinical signs (Barber, 2007).

Although this study had limitations, most notably, only 11 cases, it provides important regional epidemiological data regarding the distribution of this tumor and their survival time after the surgery.

Declarations

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Competing Interests.

The authors have no relevant financial or non-financial interest to disclose.

Animal Ethics.

The study was approved by the Institutional Animal Care and Use Committee (CEUA) of Sao Paulo State University (UNESP), School of Veterinary Medicine, Botucatu, Brazil (Approval No: 000.562).

Authors Contributions.

All authors contributed to the study and the conception design. Material preparation, data collection was performed by Daiane Cristine Lopes Duarte, César Passareli Candido Lobo and statistical analysis by Fábio Sossai Possebon. The first draft of the manuscript was written by Faviana Aimé Maza León, John Patrick Kastelic and Alessandre Hataka, and all authors commented on previous of the manuscript. All authors read and approved the final manuscript.

Data Availability.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

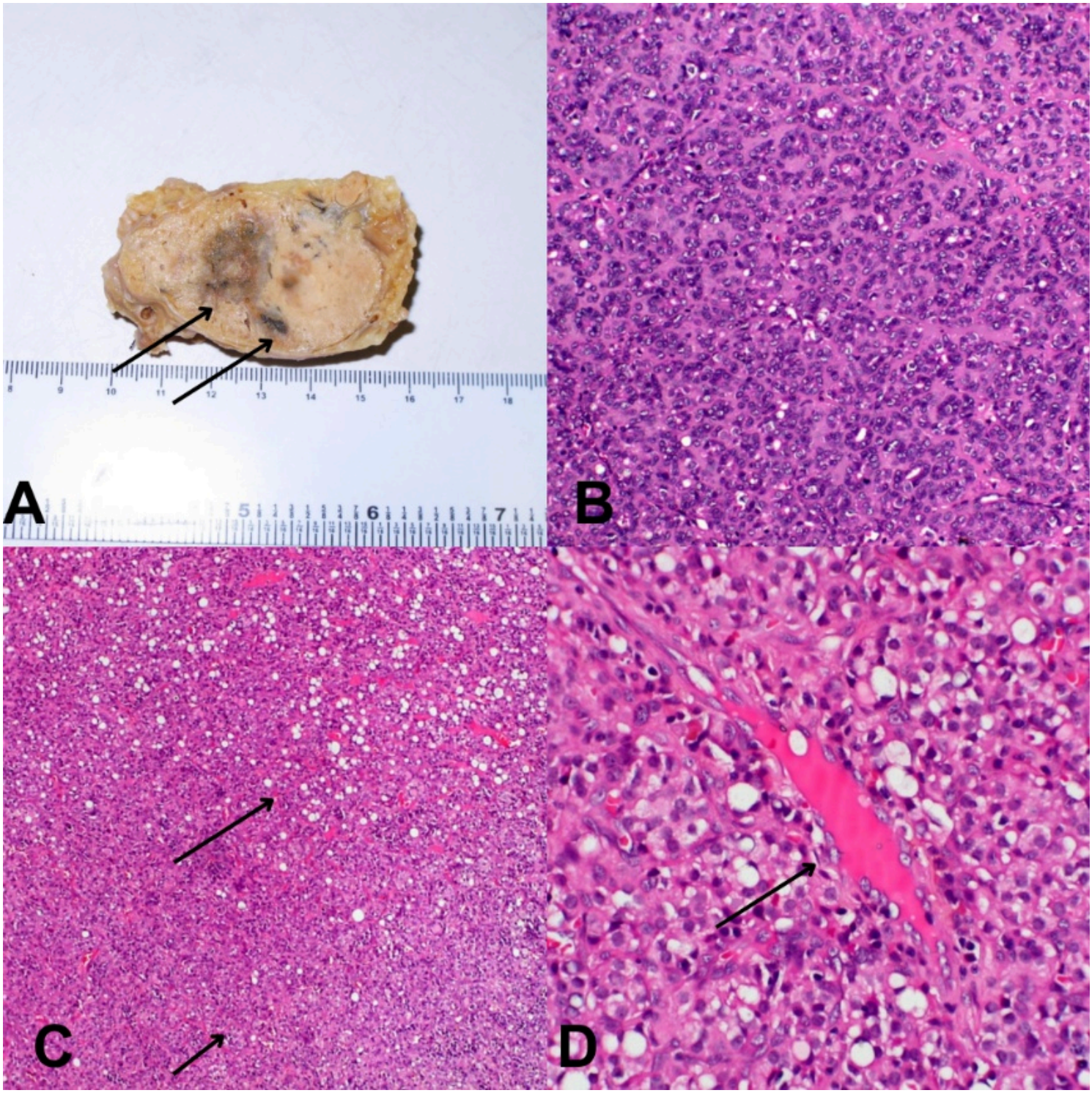


Figure 1

(A): Macroscopic appearance of compact-follicular thyroid carcinoma, area of hemorrhage and necrosis within the nodule (arrows). **(B):** Compact-follicular thyroid carcinoma. Note the balance between compact and follicular patterns (20x objective, H&E stain). **(C):** Compact-follicular thyroid carcinoma. Note the areas of compact proliferation (short arrow) and the follicular area (long arrow). **(D):** Compact-follicular thyroid carcinoma, note the thyroid follicle containing colloid (arrow) (40x objective, H&E stain).

Source. Personal achive.

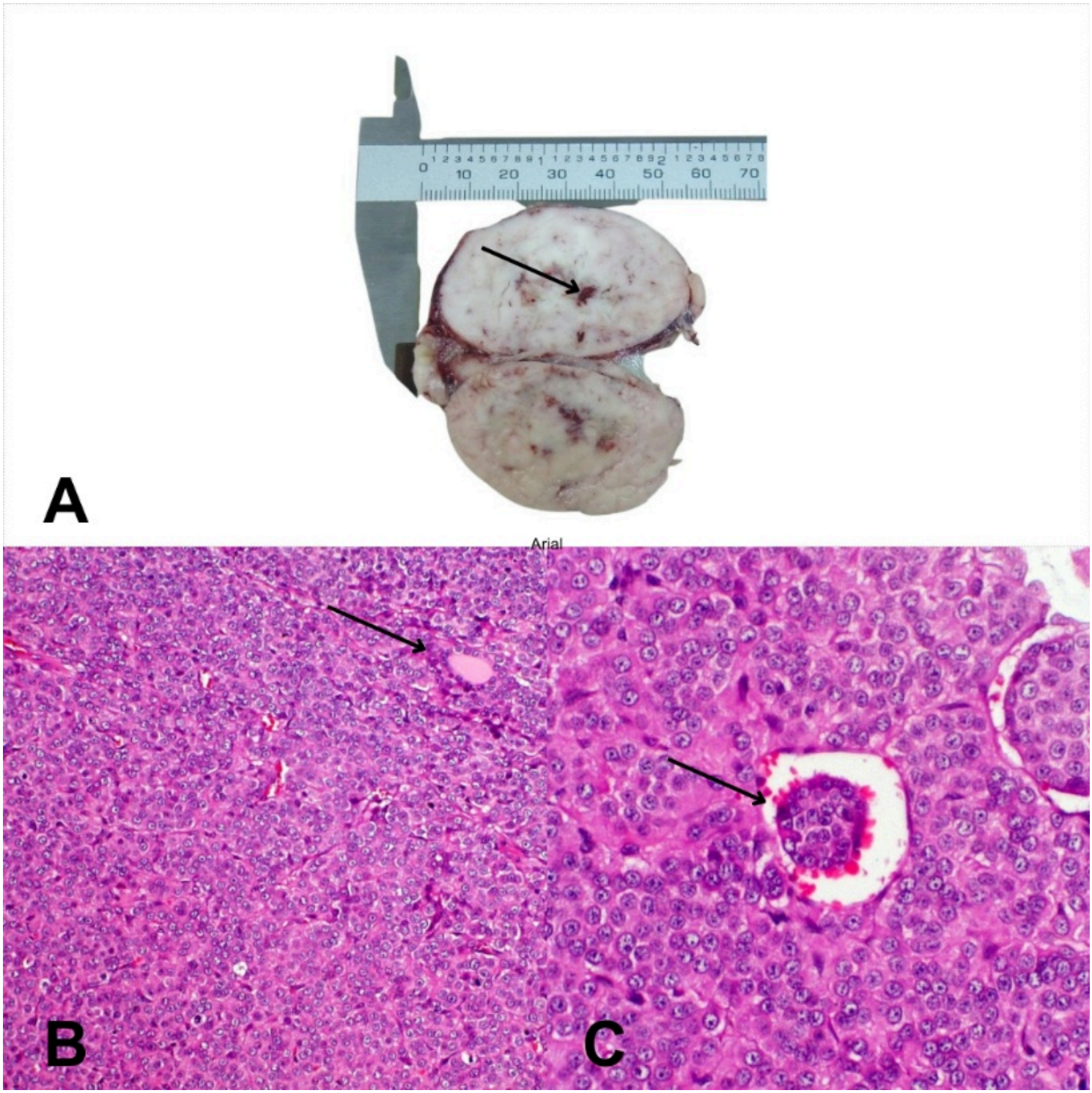


Figure 2

(A): Macroscopic appearance of the thyroid nodule, note the multilobulated and compact appearance of the lesion. In the center of the nodule, an area of hemorrhage is visible (arrow). **(B):** Compact (solid) thyroid carcinoma, neoplastic cells forming dense clusters, and a follicle containing colloid is also visible (arrow) (20x objective, H&E stain). **(C):** Compact/solid thyroid carcinoma, note the embolus of neoplastic cells (arrow) and the neoplastic cells densely grouped (40x objective, H&E stain).

Source. Personal archive.

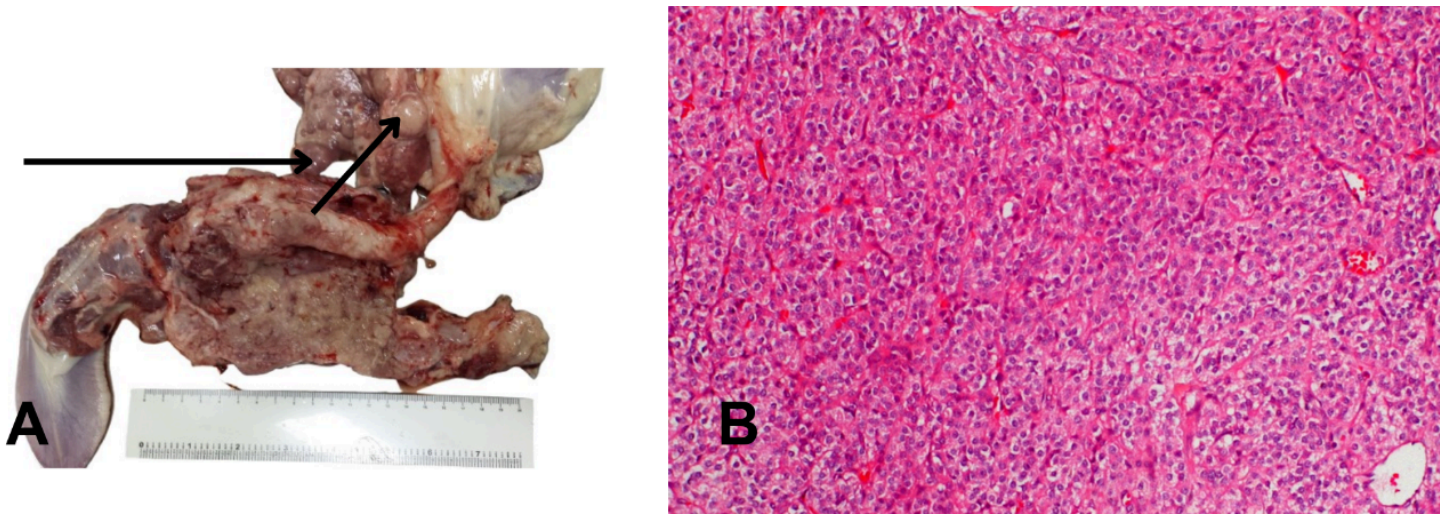


Figure 3

(A): Macroscopic appearance of compact/solid thyroid carcinoma, note the presence of metastatic nodules in the lungs (arrows). **(B):** Compact/solid thyroid carcinoma, note the densely packed neoplastic cells (20x objective, H&E stain).

Source. Personal archive.

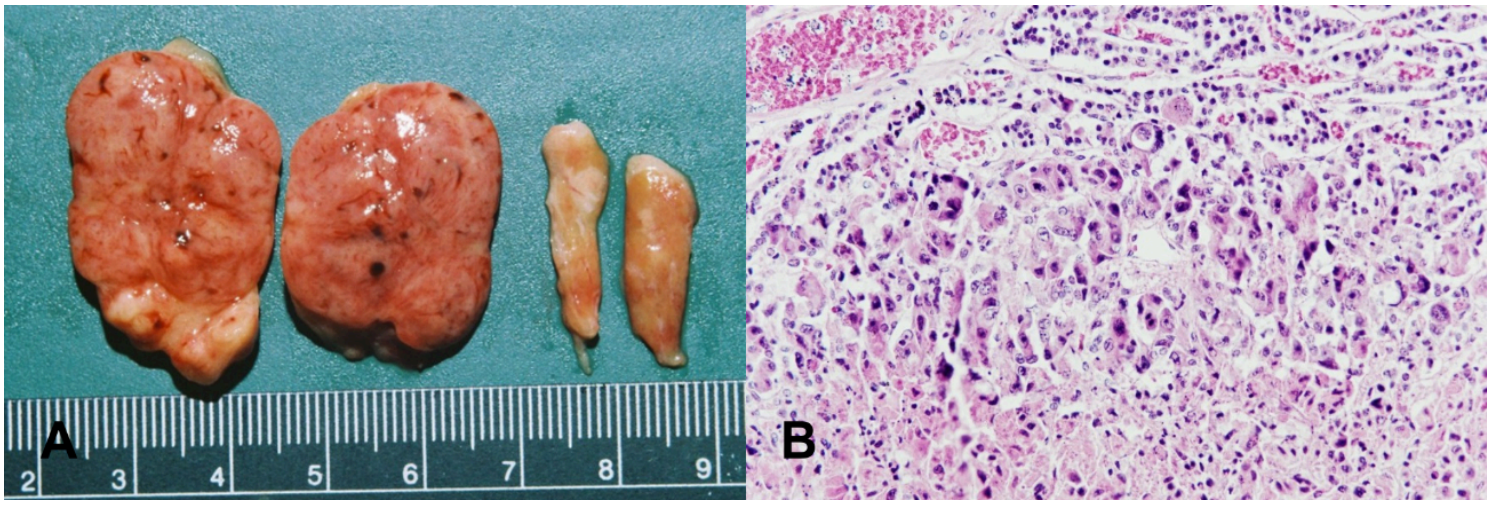


Figure 4

(A): Macroscopic appearance of undifferentiated giant cell thyroid carcinoma. **(B):**Microscopic appearance of undifferentiated giant cell thyroid carcinoma.

Source. Personal archive.

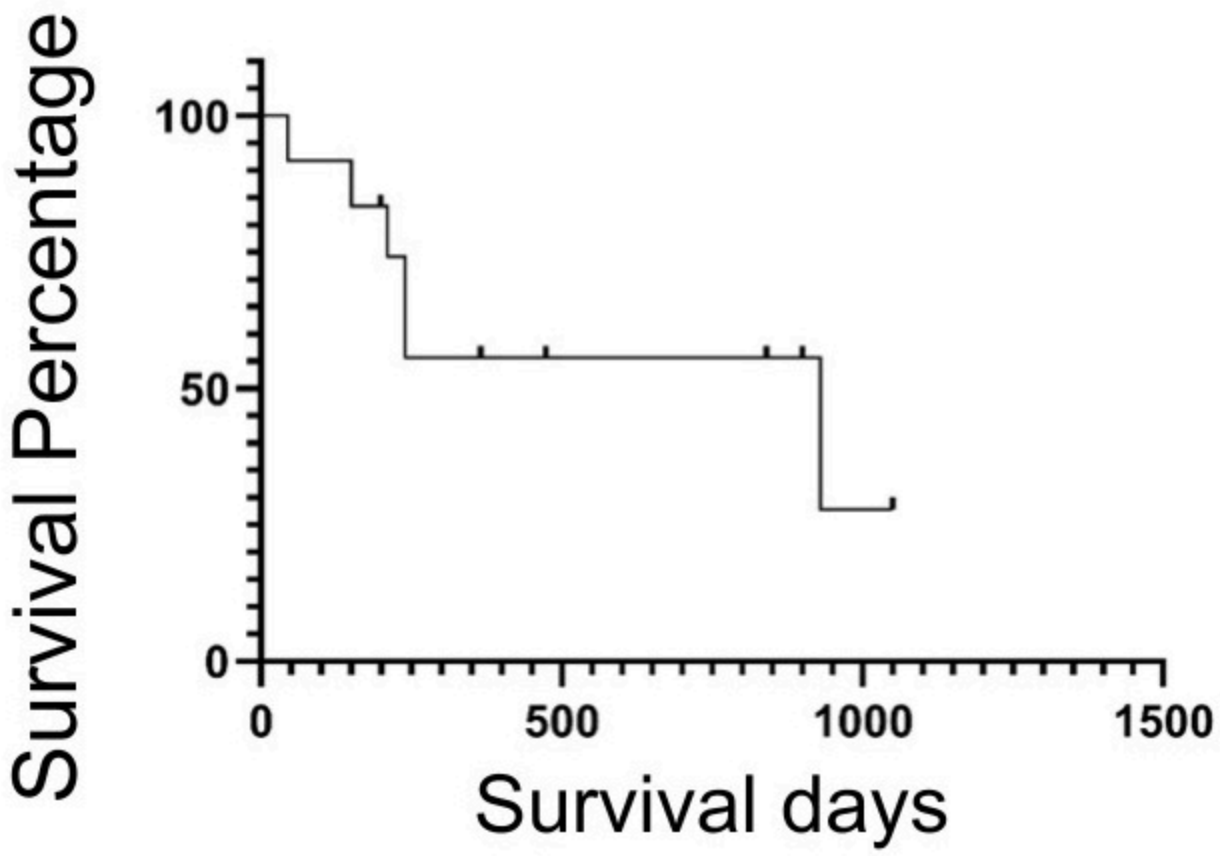


Figure 5

Survival curve (Kaplan-Meier) of seven dogs with thyroid carcinoma, the point on the graph indicates the end of the observation period for each animal.

Source. Personal archive.