J Vet Intern Med 2014;28:1560–1568

Clinical Features and Treatment Outcomes of 41 Dogs with Sublingual Ectopic Thyroid Neoplasia

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Background: Thyroid neoplasia is common in dogs, but there are few reports of dogs with ectopic, sublingual thyroid tumors.

Objectives: To describe clinical features and outcomes of dogs with ectopic, sublingual thyroid neoplasia.

Animals: Five hundred and forty-four dogs with thyroid neoplasia.

Methods: This retrospective study reviewed the medical records of dogs referred for thyroid neoplasia between 1995 and 2013. Data extracted included signalment, extent of thyroid disease (eutopic or ectopic; metastasis), serum thyroxine (T_4) concentration, treatment, and survival.

Results: Of 544 dogs with thyroid neoplasia, 41 (7.5%) dogs had ectopic sublingual thyroid tumors. The clinical features of these 41 dogs were similar to the cohort group of 503 dogs with eutopic or ectopic mediastinal thyroid tumors, but dogs with sublingual tumors were younger and less likely to have metastatic disease (15% versus 30%, $P < .05$). Of the 41 dogs, 28 received treatment: 21 with surgery (which included partial hyoidectomy in 13), 7 with radioiodine alone, and 13 with surgery followed by administration of radioiodine. Overall median survival was 562 days (range, 1-1,850 days).

Conclusions and Clinical Importance: When compared with eutopic thyroid carcinomas, ectopic sublingual thyroid tumors generally have a less aggressive biologic behavior. Many dogs have prolonged survival, even without treatment, although death because of local tumor invasiveness or metastasis can develop in some dogs. Surgical thyroidectomy, including partial hyoidectomy, is generally effective for control of local disease. Administration of radioiodine, alone or in combination with surgical treatment, is recommended for multifocal disease or metastasis.

Key words: Canine; Hyoidectomy; Hyperthyroidism; Radioactive iodine; Thyroid carcinoma.

Ectopic thyroid tissue is common in dogs, being identified in about 50% of adult dogs on necropsy examination.[1–3] During embryologic development, such ectopic tissue is formed when small groups of thyroid primordial cells separate from the main mass of developing thyroid as it migrates from the primitive pharynx (pharyngeal gut) along a midline path of descent to its normal eutopic location.[3,4] Failure of the thyroid primordium (or a portion of it) to fully descend leads to the development of lingual or sublingual ectopic thyroid tissue,[4–6] whereas additional descent of the thyroid beyond its normal cranial cervical location results in ectopic cranial mediastinal, heart base thyroid tissue, or both.[1–6]

Thyroid tumors in dogs are relatively common, representing approximately 1–3% of all neoplasia in the dog.[7–10] Tumors arising from ectopic thyroid tissue are considered relatively rare, but such ectopic thyroid neoplasia has been documented in all these locations (eg, sublingual, mediastinal, heart base) in humans[5,6] as well as dogs.[11–19] Almost all reported cases in dogs, however, represent ectopic thyroid tumors arising in the cranial mediastinal, heart base locations, or both.[11–13,15–18] In contrast, there are only a small number of reported dogs with ectopic thyroid neoplasia arising in the lingual or sublingual location,[14,19–21] and neither the prevalence nor clinical characteristics of ectopic thyroid tumors arising in this location have been described. The aim of this study was to describe the clinical features, treatment, and outcomes of 41 cases of ectopic sublingual thyroid neoplasia in dogs.

Abbreviations:

MBq	megabecquerel
mCi	millicurie
T4	thyroxine

Material and Methods

Case Selection

The medical records of all dogs referred to our clinics because of suspected thyroid neoplasia between January 1995 and July 2013 were reviewed. For inclusion in the study, the dogs had to have evidence of sublingual ectopic thyroid neoplasia on thyroid scintigraphy, with the diagnosis of thyroid neoplasia confirmed by histopathology (23 dogs) or cytology (18 dogs). Data obtained from the medical records included signalment, serum thyroxine (T_4) concentrations, scintigraphic findings, treatment modality, treatment-related complications, and survival times. Dogs were included in the category of death because of thyroid tumor-related disease if they died or were euthanized because of local extension of the tumor into adjacent structures or metastasis,

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This study was conducted at Advanced Veterinary Medical Imaging, Tustin, CA, and the Animal Endocrine Clinic, New York, NY.

Part of this study was presented in abstract form at the 33rd Annual Veterinary Medical Forum of the American College of Veterinary Internal Medicine, Seattle, WA, in 2013.

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Submitted January 10, 2014; Revised April 11, 2014; Accepted May 29, 2014.

DOI: 10.1111/jvim.12406

leading to complication including dyspnea, dysphagia, or laryngeal paralysis.

A cohort group of all other dogs that were diagnosed with thyroid neoplasia arising in other locations (eg, cervical, mediastinal) without sublingual involvement during the same time period (1995–2013) were also included to compare signalment and serum T_4 concentrations to the dogs with sublingual ectopic thyroid tumors.

Classifying Dogs into Study and Cohort Groups Based on Thyroid Scintigraphy

Thyroid scintigraphy was used to categorize the location and extent of thyroid neoplasia and to determine the tumor's uptake of radionuclide. Compared to clinically normal dogs, in which 2 small thyroid lobes on either side of the trachea can be visualized in the cervical region (Fig 1A),[22,23] the study group of dogs with sublingual ectopic thyroid had abnormal thyroid uptake located near the ventral midline and cranial to the larynx (Fig 1B). In these dogs, the extent of disease was defined as localized if only sublingual thyroid tumor tissue was visualized. Dogs with additional discrete areas of abnormal radionuclide uptake in the ventral neck or cranial mediastinum were defined as having multicentric primary disease. Dogs with abnormal radionuclide uptake in the lungs, but not the cranial mediastinum, were defined as having pulmonary metastatic disease.

Dogs with thyroid neoplasia were included in the cohort group if thyroid scintigraphy confirmed eutopic thyroid enlargement in the cervical region (Fig 1C), or if thyroid scintigraphy confirmed radionuclide uptake in ectopic thyroid tissue arising in the cranial mediastinum (Fig 1D). Again, dogs of the cohort group that had abnormal radionuclide uptake in the lungs or regional lymph nodes were defined as having metastatic disease. None of the dogs in this cohort group had evidence of sublingual thyroid involvement.

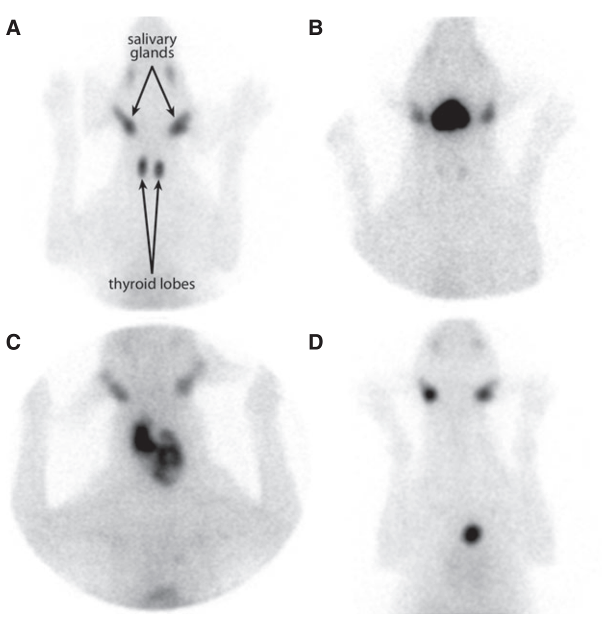

Fig 1. Ventral thyroid scintigraphic images of normal dogs and dogs with thyroid neoplasia. **(A)** Normal thyroid gland; **(B)** ectopic sublingual thyroid neoplasia; **(C)** eutopic thyroid neoplasia involving both cervical thyroid lobes; and **(D)** ectopic cranial mediastinal thyroid neoplasia. Normal parotid salivary glands (evident on all thyroid scans), as well as both normal thyroid lobes, are labeled in panel A. In the normal dog, notice the similar (1 : 1) radionuclide uptake in the normal lobes and salivary glands, whereas some dogs with functional thyroid tumors clearly show increased uptake of the radionuclide, as compared to the salivary tissue.

Thyroid Scintigraphy, Determination of Thyroid Counts, and Thyroid-to-Salivary Ratio

Scintigraphy was performed 20 minutes after intravenous administration of 0.5 mCi/Kg (18.5 MBq/kg) sodium pertechnetate ($Na^{99m}TcO_4^-$).[a,b] Images were acquired using a gamma camera[c] set to a photopeak of 140 KeV with a 20% window and fitted with a low-energy, all-purpose collimator. A 256 × 256 matrix was utilized and images were acquired for a total of 250,000 counts. DICOM images were acquired and evaluated by dedicated nuclear medicine[d] and DICOM viewing[e] software.

After image acquisition in the study dogs, regions of interest were drawn manually around the ectopic sublingual tumor and compared to the salivary gland activity. A thyroid-to-salivary ratio (T/S ratio) was then calculated by dividing the average thyroid tumor count density (total thyroid counts/total thyroid pixels) by the salivary count density (total salivary counts/total salivary gland pixels), as previously described.[22] In clinically normal dogs, the T/S ratio ranges from 0.9 to 2.2.[22,23] For cases of multicentric or metastatic disease, normal to increased radionuclide uptake was used as one of our criteria for using radioiodine as part of treatment.

For dogs treated with radioactive iodine (^{131}I),[a] response to treatment was evaluated >30 days after treatment with repeat thyroid scintigraphy, using both visual examination as well as calculation of the posttreatment T/S ratio. In addition, response to treatment was quantified by calculating the difference between the background-corrected, mean pre- and posttreatment total thyroid counts, divided by the background-corrected mean pretreatment thyroid counts.[24]

Statistical Analyses

Data were assessed for normality by the D'Agostino-Pearson normality test and by visual inspection of graphic plots.[25] The assumption of Gaussian distribution was not met and therefore nonparametric testing was used.[26,27] Comparisons of signalment data between the study and cohort groups of dogs were performed by use of the Mann-Whitney test and Fisher's exact test, with results reported as median (range). The Wilcoxon signed-rank test was used to determine the difference in the median T/S ratios before and after ^{131}I treatment. The Chi-square test was used to determine whether differences existed in the proportion of the dogs with metastasis or multicentric thyroid disease treated with surgery, radioiodine, or both.

Survival times are presented as median (range) with the date of the pretreatment scintigraphic scan defined as day 1. Kaplan-Meier survival analysis was performed to compare survival between treatment modalities; between dogs with and without metastatic disease; between dogs with and without high serum T_4 concentrations; and between dogs with and without low serum T_4 concentrations. Survival analysis[28] was performed by proprietary statistical software.[f] For all statistical analyses, values of $P < .05$ were considered significant.

Results

Thyroid Scintigraphic Findings in Study and Cohort Groups

Of the 544 cases of thyroid neoplasia reviewed, 41 (7.5%) dogs had sublingual disease. Of these, 29

(70.7%) had localized disease confined to the sublingual site. Twelve (29.3%) of the 41 dogs had multicentric primary tumors; of these, 9 had abnormal radionuclide uptake in the ventral neck (eutopic disease) in addition to the sublingual disease, 1 dog had additional abnormal radionuclide uptake in the cranial mediastinum (ectopic mediastinal disease), and 2 had additional abnormal radionuclide uptake in both the ventral neck and cranial mediastinum. Finally, 6 (14.6%) of the 41 dogs with sublingual tumors also had pulmonary metastatic disease; 2 of these had primary disease confined to the sublingual site, whereas 4 dogs had multicentric primary disease.

In the cohort group of 504 dogs with primary thyroid neoplasia in other locations other than the sublingual site, 474 (94%) dogs had eutopic thyroid neoplasia, 14 (2.8%) had only ectopic mediastinal disease, and 16 (3.2%) had concurrent ventral cervical and mediastinal disease. Finally, 151 (30%) dogs in the cohort group had metastatic disease to the lungs (77 dogs), regional lymph nodes (108 dogs), or both (24 dogs).

Differences in Signalment and T_4 Concentrations between Study and Cohort Groups

Males and females were approximately equally represented in both the dogs with ectopic sublingual tumors (23 females, 18 males) and the cohort group of dogs with thyroid tumors in other locations (247 females, 256 males; $P = .62$). Nearly all dogs of both groups were neutered, with only 1 dog in the sublingual ectopic group being sexually intact. Median body weight was 30 kg (range, 5.4–70 kg) in dogs with sublingual disease and 26.8 kg (2.3–62 kg) in the cohort group ($P = .76$). The median age of the dogs with ectopic sublingual tumors (9.1 years; 4–15 years) was significantly younger than the age of the cohort group (11 years; 4–18 years; $P = .01$). There were no significant breed differences between the 2 groups of dogs with thyroid neoplasia. Of the 41 dogs with sublingual disease, 14 of the dogs (34%) were mixed breed, and 13 (31%) were Labrador or Golden Retriever. Similarly, of the dogs in the cohort group, 117 dogs (23%) were mixed breed, and 115 (23%) were Labrador or Golden Retrievers.

Ten (29%) of the 41 dogs with sublingual thyroid tumors and 146 (29%) of the 504 dogs in the cohort group had serum T_4 concentrations above the reference range limits. There was no significant difference in the prevalence of hyperthyroidism between the study or cohort group.

Dogs with ectopic sublingual thyroid tumors, however, were less likely than dogs in the cohort group to have metastatic disease at the time of diagnosis (14.6% versus 30%; $P = .04$).

Fine-Needle Aspiration Cytology and Histopathology

Histopathologic examination of tumor tissue from 23 of the 41 dogs with sublingual thyroid tumors revealed thyroid adenocarcinoma in all of these cases. The histologic type of thyroid carcinoma was follicular carcinoma in 13 dogs and mixed compact-follicular in 10 dogs. None of the dogs were considered to have compact thyroid adenocarcinoma or medullary carcinoma. In none of these cases was immunocytochemistry used, however, to differentiate a follicular cell origin of the tumor from C-cell origin (medullary carcinoma).

Fine-needle aspiration cytology was performed in remaining 18 dogs. In most of these dogs, it was not possible to differentiate thyroid adenoma from adenocarcinoma, nor was it possible to exclude medullary carcinoma with cytology.

Treatment and Survival Time

Twenty-eight of the 41 dogs with sublingual thyroid tumors were treated. Of these, 8 were treated with surgical excision alone, 7 were treated with radioactive iodine alone, and 13 were treated with surgery followed by radioiodine. In total, 21 dogs had surgical excision as part of their treatment; of these, partial hyoidectomy[14,20] was performed as part of the surgical excision in 13 dogs.

Of the 21 dogs treated with surgery, 17 dogs had repeat thyroid scintigraphy done as part of the follow-up. Based on these scintigraphy findings, excision was regarded as complete in only 9 (53%) of the 17 dogs and as incomplete in the remaining 8.

Of the 13 dogs that had partial hyoidectomies as part of the surgical treatment, 9 were available for postsurgical thyroid scintigraphy. In these 9 dogs that had partial hyoidectomy, 8 (89%) had complete surgical excision of their sublingual disease (Fig 2). Of the remaining 8 surgically treated dogs that did not have partial hyoidectomies, all were available for postsurgical thyroid scintigraphy. Of these, 6 of these 8 dogs (75%) failed to have complete surgical excision of their disease (Fig 3). Only 2 dogs (25%) had sublingual disease independent of the basihyoid bone, allowing for complete surgical excision without partial hyoidectomy.

There were no reported complications associated with surgery, regardless of whether the surgical procedure included partial hyoidectomy. Specifically, dysphagia, dyspnea, and dysphonia were not reported for any of the 21 dogs treated with surgery.

Radioiodine was administered in 20 of the dogs after 2 weeks on an iodine-restricted diet, using a median dose of 3.5 mCi/kg (130 MBq/kg) for dogs with gross scintigraphic disease and a median dose of 2.0 mCi/kg (75 MB/kg) for dogs with no gross scintigraphic disease. Of these dogs treated with radioiodine, follow-up thyroid scintigraphy was performed in 3 dogs treated with radioiodine alone and in 7 dogs treated with surgery followed by radioiodine. After treatment, the median T/S ratio in these 10 dogs decreased from 4.0 to 0.36 ($P = .002$). Technetium uptake (ie, background-corrected thyroid counts) in these 10 dogs decreased by a median of 97% (range,

Fig 2. Ventral thyroid scintigraphic image **(A)** of a dog with ectopic sublingual thyroid neoplasia at time of diagnosis; **(B)** at 1 month after successful surgical treatment (which included partial hyoidectomy); and **(C)** at 1 month after additional ablative radioiodine treatment.

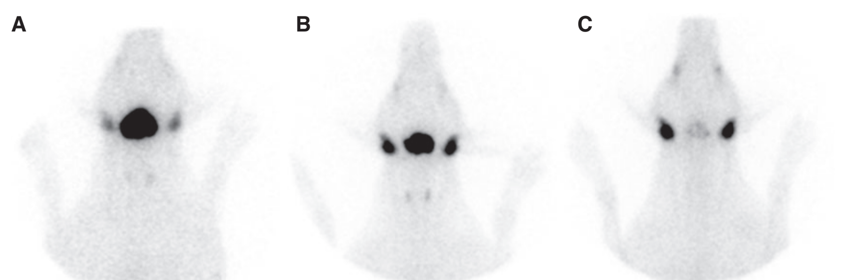

Fig 3. Ventral thyroid scintigraphic image **(A)** of a dog with ectopic sublingual thyroid neoplasia at time of diagnosis; **(B)** at 1 month after unsuccessful surgical treatment (partial hyoidectomy not performed); and **(C)** at 1 month after radioiodine treatment. Response to radioiodine treatment, measured by the reduction in percent radionuclide thyroid uptake, was determined to be 94%.

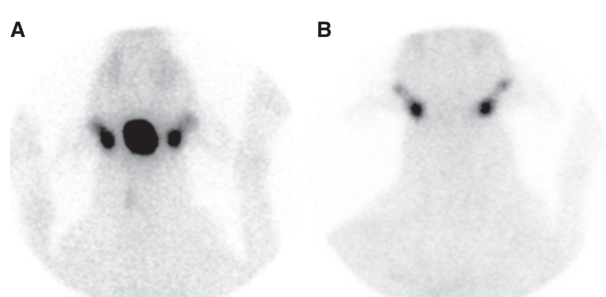

Fig 4. Ventral thyroid scintigraphic image **(A)** of a dog with ectopic sublingual thyroid neoplasia at presentation; and **(B)** at 1 month after radioiodine treatment. Response to radioiodine treatment, measured by the reduction in percent radionuclide uptake by the thyroid mass, was determined to be 100%.

42–100%) compared to preradioiodine thyroid counts (Figs 3, 4).

In 13 of the 41 dogs, the owners declined treatment because of personal or financial reasons. All of these dogs had fine-needle aspiration cytology performed, but none had histopathologic examination of thyroid tumor tissue. Of these 13 dogs, only 1 had evidence of pulmonary metastasis and that dog was lost to follow-up after only 19 days. Only 1 of these dogs was mildly hyperthyroid, and that dog was lost to follow-up after 39 days. Of the remaining 11 dogs, all were considered to have relatively mild disease (limited to sublingual site in 9), and only 1 dog was euthanized (670 days after diagnosis) because of thyroid tumor-related complications. Of these untreated dogs, 8 were known to be alive for at least 1 year after initial evaluation.

Overall, the median survival for all 41 dogs with ectopic sublingual thyroid tumors was 562 days (range, 1–1,850 days). Of these, 9 dogs (24.3%) died of causes related to their thyroid neoplasia (ie, dyspnea, dysphagia, or laryngeal paralysis) at a median time of 537 days after initial scintigraphy (range 224–1,782 days), 3 died of unrelated malignancy (322, 1,104, and 1,850 days), 9 died or were euthanized at a median time of 918 days (range, 537–1,218 days) because of miscellaneous conditions unrelated to the thyroid neoplasia, and 20 were alive at the time of follow-up (median, 416 days; range, 19–1,492 days).

Median survival times did not vary significantly (P = .16) regardless of whether dogs were treated with radioiodine alone (347 days; range, 75–1,104 days), surgery alone (1,160 days; range, 1–1,782 days), both surgery and radioiodine (976 days; range, 322–1,850 days), or were untreated (670 days; range, 1–1,072 days). However, median survival time in the 21 dogs treated with surgery was significantly longer than the 20 that did not receive surgical treatment (873 days versus 481 days; P = .018).

The medium survival time in the 6 dogs that had metastatic disease was less than the time in those 35 dogs without metastatic disease (278 days versus 573 days), but this difference was not significant

(P = .31). We did find substantial treatment bias according to extent of disease, as evidenced by the fact that radioiodine was administered to 5 of the 6 (83%) dogs with metastatic disease, but to only 15 of the 35 (43%) dogs without metastasis (P = .07). In addition, a significant difference (P = .015) existed in the incidence of metastatic or multicentric disease among the dogs treated with surgery alone (none of 8 dogs; 0%) versus the dogs treated with radioiodine alone (5 of 7 dogs; 71.4%) and the dogs treated with both surgery and radioiodine (5 of 13 dogs; 38%).

Discussion

Despite the paucity of reports of sublingual ectopic thyroid neoplasia, this case series demonstrates that the sublingual location is involved in approximately 7.5% of dogs with clinically detected thyroid tumors. This is important because thyroid neoplasia might be overlooked as a differential diagnosis for sublingual tumors, and the prognosis is substantially better for dogs with ectopic sublingual thyroid neoplasia than with many other oral tumors.[29–32] The differential diagnoses for a mass centered on the basihyoid region include both primary bone and soft tissue sarcomas, as well as primary laryngeal carcinomas infiltrating the surrounding hyoid region.[32] These tumors, as well as many of the other tumors commonly identified in the oropharynx or sublingual region, including squamous cell carcinoma and oral malignant melanoma, have a poor prognosis and short survival times.[29–32] In contrast, the median survival time of dogs in this case series was nearly 1.5 years regardless of the presence of metastatic disease at the time of diagnosis. Thyroid neoplasia should be included in the differential diagnoses considered for tumors of the ventral oropharynx, and might have a better outcome than other tumors in this location.

When the clinical features of these 41 dogs with ectopic sublingual thyroid tumors were compared to those of the cohort group of dogs with eutopic thyroid carcinomas, we found no difference in the sex and neuter status, body weight, size, or prevalence of hyperthyroidism between these 2 groups of dogs. However, the dogs with sublingual tumors were younger and less likely to have metastatic disease (15% versus 30%) than the dogs with eutopic thyroid carcinomas. It is possible that dogs with sublingual tumors presented earlier for treatment because mass lesions involving the sublingual region are easier for the owner and veterinarian to see or palpate. In addition, these dogs with ectopic sublingual tumors tended to have a better prognosis than most dogs with eutopic tumors, as exemplified by the prolonged survival time in many of these dogs, even some that did not receive any treatment.

The diagnosis of ectopic thyroid neoplasia in the 41 dogs of this study was made on the basis of thyroid scintigraphy, as well as results of either fine-needle aspiration (FNA) cytology or histopathologic examination of neoplastic tissue. Although one study of dogs with thyroid carcinoma reported a close agreement in cytologic and histopathologic findings,[33] FNA cytology is often discounted as being unrewarding and of limited value for diagnosis of canine thyroid carcinoma.[9,34] Malignant tumors of follicular origin, even when they show aggressive clinical behavior, will generally show only limited evidence for malignancy on cytology.[35] Aspirates from canine thyroid tumors (both adenomas and carcinomas) are usually bloody and often poorly cellular, as neoplastic thyroid tissue has a higher vascular density than normal thyroid parenchyma.[34,35] In addition, the neoplastic cells closely resemble those aspirated from normal thyroid tissue and only rarely show signs of moderate to severe atypica.[35] Therefore, differentiating thyroid adenoma and carcinoma on a cytologic basis will not be possible in many dogs. Overall, the main value of FNA cytology may lie its ability to verify that the neoplastic mass is of thyroid origin rather than as a tool to confirm malignancy.[10,35]

In dogs, most thyroid tumors detected clinically are malignant and arise from the follicular epithelium; these tumors are usually detected as large, invasive, fixed, and poorly circumscribed cervical masses, which generally show aggressive clinical behavior and are associated with a guarded to poor prognosis.[9,10,34] Thyroid adenomas, on the other hand, are reported to comprise about 30–40% of canine thyroid tumors at necropsy.[7,8] However, as these benign tumors are usually small and often do not cause hyperthyroidism, they may go undiagnosed by clinicians. In these 41 dogs, thyroid carcinoma was confirmed in all 23 dogs in which histopathology was done. In the remaining 18 dogs, 4 had evidence of metastasis on thyroid scintigraphy, which also made carcinoma highly likely. However, it is possible that at least some of the remaining 14 dogs had thyroid adenoma, as they did not have histopathology done and no evidence of metastasis was seen on thyroid scintigraphy. If some of these ectopic masses were benign, that could explain the prolonged survival time seen in some of these dogs that did not receive any treatment.

Although most canine thyroid tumors arise from the follicular epithelium,[8–10] up to a third of thyroid tumors may arise from the parafollicular cells (C-cells) and may be difficult to distinguish from follicular tumors with routine histopathology alone.[8,36,37] Immunocytochemistry studies are helpful in differentiating follicular from C-cell tumors, as follicular tumors stain positively for thyroglobulin[38,39] and C-cell tumors (ie, thyroid medullary carcinomas) show immunoreactivity to calcitonin, calcitonin gene-related peptide, or both.[36–39] In the dog, differentiation between follicular and C-cell tumors may have clinical relevance, as evidence suggests that medullary tumors may be less invasive, with a lower potential for metastasis, than are thyroid follicular tumors.[36] This gives rise to the question: could some of these dogs with ectopic sublingual tumors actually have been C-cell (medullary carcinomas), rather than thyroid follicular tumors? Could this explain the lower incidence of metastasis and less aggressive behavior, as compared to our cohort group of dogs with eutopic thyroid tumors? Although certainly possible, given that immunocytochemical differentiation was not performed in any of the ectopic thyroid tumors in this report, ectopic medullary carcinoma is unlikely. First of all, thyroid scintigraphy demonstrated that almost all of these dogs (36 of 41) displayed a normal to increased uptake of pertechnetate by the ectopic thyroid tumor. This is a characteristic feature of thyroid follicular tumors (see below), whereas thyroid medullary tumors generally cannot be imaged with either pertechnetate or radioiodine.[40] In addition, as the embryology of C-cells differs from that of the thyroid follicular cell, it cannot be expected that C-cells would also migrate to ectopic sites.[5,6] In support of that, ectopic thyroid tissue characteristically shows negative immunostaining for calcitonin,[41–44] and medullary thyroid tumors arising in ectopic sites have not been described in dogs.[12,18,36–39,42,45,46] Similarly, in human patients, only a single case report of medullary carcinoma arising in an ectopic site has been reported,[47] although ectopic thyroid disease is not uncommon, with over 500 reported cases described.[5,6]

Thyroid scintigraphy provides valuable diagnostic information in dogs with suspected thyroid neoplasia and was used in these dogs to help confirm that the sublingual mass lesions were indeed of thyroid origin. The presence in multiple locations of thyroid tumor in some of these dogs with ectopic sublingual disease, as well as the dogs in the cohort group, underlines the importance of preoperative staging in this disease. Scintigraphy is generally considered to be the thyroid imaging technique of choice for specifically detecting and delineating functioning thyroid tumor tissue[22,23] and is especially useful for detecting ectopic thyroid tumors or metastatic thyroid disease.[23,45,48,49] Thyroid scintigraphy can also play an integral role in the management and follow-up of dogs treated with surgery or radioiodine. For these reasons, thyroid scintigraphy represents our preferred diagnostic imaging modality for the initial staging of dogs with suspected thyroid neoplasia.

Contrast-enhanced computed tomography (CT) has been described as a highly specific way to distinguish thyroid tumors from other cervical masses,[50] and CT is a more sensitive modality to detect pulmonary metastatic nodules than conventional radiography.[51] Recently, the CT characteristics of 8 dogs with ectopic sublingual thyroid carcinoma were reported;[21] in that study, these tumors were associated with severe lysis of the basihyoid bone, with infiltration of the laryngeal wall or laryngeal lumen, sometimes with metastasis. Based on these characteristic features, it was concluded that CT is strongly indicated for evaluation of dogs with cranioventral cervical masses, as CT identifies the most probable origin of the tumor and can be used for treatment planning.[21] While there is no doubt that use of CT has facilitated the diagnosis and staging of head and neck tumors, there are potential problems with the routine use of CT for evaluation dogs with thyroidal neoplasia. Contrast-enhanced CT involves the use of iodinated contrast agents. Iodinated contrast agents contain variable amounts of free iodide,[52] which can persist in tissues for weeks or months after administration.[53,54]This circulating stable iodide is also taken up by the thyroid gland, and can therefore reduce the subsequent thyroid uptake of both technetium and radioiodine, an effect that can persist for several months after the administration of iodinated contrast agents.[52–54] Therefore, this free iodide-load of contrast media injections interferes with iodide uptake in the thyroid, compromises diagnostic thyroid scintigraphy, and makes radioiodine treatment for thyroid malignancy less effective. Although this inhibitory effect of iodinated contrast agents on subsequent thyroid uptake of technetium and radioiodine has not been thoroughly documented in dogs, there is no strong reason to expect that dogs would be unaffected by this effect. Therefore, we recommend that veterinarians avoid contrast-enhanced CT in tumors of the tongue, ventral neck, and cranial mediastinum unless thyroid neoplasia or the later use of thyroid scintigraphy or radioiodine has been ruled out.

Recent reports have shown magnetic resonance imaging (MRI) to be preferred over CT for the preoperative diagnosis and staging of clinically suspected thyroid carcinomas.[50] When compared with CT, MRI yielded results that more closely matched histology for evidence of local tissue invasion.[50] Unlike CT, MRI will not interfere with subsequent thyroid scintigraphy or radioiodine treatment as no iodinated contrast is administered.

The ideal treatment for dogs with ectopic sublingual thyroid neoplasia is not known, but may include surgical excision, use of ablative doses of radioiodine, external radiotherapy, or chemotherapy.[2,16,30,37–40] In our study, most dogs with localized sublingual thyroid tumors (no metastasis or multicentric disease) could be controlled or even cured with surgical incision. However, these thyroid tumors frequently invaded the hyoid apparatus, necessitating partial hyoidectomy to attain regional control. Hyoidectomy was not associated with substantial morbidity or mortality. These dogs were swallowing normally at the time of discharge, typically within 3 days of surgery. This is similar to the experience of others, with adverse effects limited to mild or moderate postoperative swelling.[14,19,20] Partial hyoidectomy was first suggested in humans as part of the removal of thyroglossal duct cysts;[55] because the thyroglossal duct is friable and typically travels through rather than around the basihyoid bone, it becomes very difficult to dissect the tissue away completely as it approaches the basihyoid bone. In dogs with ectopic sublingual thyroid tumors that are treated surgically, the need for partial hyoidectomy should be anticipated to ensure complete excision of tumor tissue that may invade the basihyoid bone.

In dogs with ectopic sublingual tumors that also have multicentric disease or metastasis, use of surgery alone is unlikely to result in cure. If the tumor is functional and can be demonstrated to have normal or enhanced thyroid uptake of radionuclide, high-dose radioiodine can be considered in such cases. If the thyroid uptake is low, or radioiodine is not available or an option, then surgery followed by external beam radiation treatment or chemotherapy could be considered.[9,10,56,57]

The treatment results reported here in these dogs with ectopic sublingual thyroid tumors cannot be directly compared with other studies because these dogs included a mix of cases with localized and multicentric disease, both with and without metastatic disease, treated with a variety of treatment combinations, but are within the range of outcomes documented for dogs with eutopic thyroid neoplasia. Around 20% of these dogs with sublingual thyroid tumors died of thyroid neoplasia-related problems (associated with the local invasion of primary tumor or pulmonary metastasis) during the follow-up. This is similar to reports of dogs with thyroid neoplasia in other locations,[56–58] highlighting the importance of systemic treatment as a component of treatment in dogs with thyroid neoplasia. Prospective clinical trials are needed to document the need for and relative efficacy of currently recommended treatments for dogs with sublingual thyroid tumors.

However, our results also show long survival (median, greater than 1 year) in dogs with untreated sublingual thyroid tumors. This differs from the results of another retrospective study of dogs with eutopic thyroid neoplasia, which documented a median survival time of only 3 months in untreated dogs.[59] It is important to note that only 2 (15%) of these untreated dogs had multicentric disease, and that none that survived more than a year had any evidence of local invasion or metastasis. Again, these dogs might have had thyroid adenoma rather than carcinoma, as none had histopathologic examination of their neoplastic tissue. Alternatively, these dogs could just represent milder or earlier cases of thyroid carcinoma, and it might be that some ectopic tumors simply represent a less aggressive type of thyroid tumor in dogs. In support of that, only 1 dog was euthanized (670 days after diagnosis) because of thyroid tumor-related complications, and over 60% of these untreated dogs were known to be alive for at least 1 year after initial evaluation.

In this study, the group of dogs with sublingual tumors was significantly younger and less likely to have metastatic disease at the time of diagnosis than the cohort group. It is possible that dogs with sublingual tumors presented earlier for treatment because mass lesions involving the sublingual region are easier for the owner and veterinarian to see or palpate. This could explain their younger age and lower prevalence of metastatic disease compared with the cohort group. This study includes several limitations, including the retrospective nature of the study, which led to confounding in some instances. For example, dogs with more advanced disease (eg, local invasion, regional, or distant metastasis) were more likely to be treated with radioiodine than those dogs without metastasis, which limited our ability to assess the extent of disease on survival. Conversely, however, it appears that multimodal treatment of these dogs with ectopic sublingual tumors provides effective treatment and long-survival times even in cases with metastasis. Finally, the numbers of dogs included was small because ectopic sublingual thyroid disease is not a very common clinical entity. As a result, the statistical analyses might have suffered from inadequate power and the null hypothesis might have been falsely accepted.

Footnotes

[a] Cardinal Health Nuclear Pharmacy Services, Placentia, CA

[b] Nuclear Diagnostic Products, Rockaway Township, NJ

[c] Pho/Gamma LFOV; Searle Radiographics Inc, Des Plaines, IL or MaxiCamera 400 Nuclear Gamma Camera; GE Medical Systems, Pittsburgh, PA

[d] Nuclear Mac; Scientific Imaging, Inc, Crested Butte, CO

[e] OsiriX; Pixmeo, Geneva, Switzerland

[f] GraphPad Prism, version 6.0; GraphPad Software, La Jolla, CA

Acknowledgments

Manuscript preparation, statistical analysis, and editorial assistance were provided by Kurt Verkest of VetWrite (vetwrite@gmail.com).

This project was self-funded.

Conflict of Interest Declaration: Authors disclose no conflict of interest.

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