

THYROID NODULES, BUMPS, & LUMPS: WHEN IS MEDICAL THERAPY A USEFUL OPTION?

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THYROID NODULES IN HUMAN PATIENTS

In humans, thyroid nodules are common, occurring in over half of individuals over 50 years of age. Over 95% of these thyroid nodules are benign, small to moderate in size, and are not associated with clinical or biochemical signs of hyperthyroidism. Some of these patients that present with a single thyroid nodule are later found to have many benign enlarged nodules within the thyroid (ie, multinodular goiter), some of which will develop signs of hyperthyroidism (toxic nodular goiter; Plummer's disease). Although the underlying cause of most human thyroid nodules is not known, a low-iodine diet, Hashimoto's thyroiditis, or prior radiation treatment can contribute to nodule development.

The most common medical treatment used in management of thyroid nodules in human patients is thyroid suppressive therapy, in which L-thyroxine is used to suppress pituitary TSH secretion and slow the growth of the thyroid nodule. In all human patients found to have a thyroid nodule, a major concern is the possibility of thyroid cancer, in which more aggressive therapy is required. The finding that thyroid replacement results in shrinkage of the nodule makes thyroid cancer less likely. Unfortunately, there is not clear evidence that treatment with L-thyroxine consistently shrinks thyroid nodules or even that shrinking small, benign nodules is necessary in most patients.

THYROID NODULE/MASSES IN DOGS AND CATS

In most dogs and cats that present with a thyroid nodule or cervical mass, the pathogenesis and treatment are quite different from that of the human patient with a thyroid nodule (see Table 1). As discussed below, administration of T4 to suppress the goiter or nodule, as sometimes used in humans, is successfully used in some conditions (eg, some forms of congenital hypothyroidism). Most of the time, however, other treatments must be used, as dictated by the final diagnosis.

The most common situation for veterinarians to find a thyroid nodule would be in the middle to older cat. Some of these nodules are thyroid in origin; others are nonthyroidal in origin

(eg, parathyroid or lymphatic nodules). Some are functional, some are non-functional or in the process of evolving toward overt hyperthyroidism (See Table 1). Indeed, the presence of an incidental mass in the cervical/thyroid area can sometimes be an enigma in companion animal practice. Surgical biopsy may not be justified if lesions are non-functional, which is often the case early in the clinical course when T4 determinations are in the reference interval.

Hyperthyroidism in Cats

Since hyperthyroidism was first reported 31 years ago, the prevalence of thyroidal nodules and the associated hyperthyroid state has been detected at an increasing frequency, with a prevalence now estimated to be as high as 2% of cats in general practice. Histopathology of affected thyroids usually reveals thyroid hyperplasia or benign thyroid adenoma; however, in a small percentage of cats (especially those with long-standing hyperthyroidism management with antithyroid drugs), thyroid adenocarcinoma is diagnosed. The time course of the progression of normal feline thyrocytes to hyperfunctioning adenomatous hyperplasia/adenoma and then to thyroid carcinoma is not known.

The presence of a palpable thyroid nodule is one of the cornerstones in securing a diagnosis of hyperthyroidism, but a functional hyperthyroid state must be confirmed on the basis of other characteristic clinical features, (ie, weight loss in the face of a good appetite). The diagnosis of hyperthyroidism can usually be confirmed by measurement of a single serum T4 concentration. In some cats with early hyperthyroidism or which have concurrent nonthyroidal disease, the T4 concentration may intermittently fluctuate into the normal range. If the T4 is high-normal or borderline, diagnostic options include repeating the T4 level or measuring a free T4 concentration (by equilibrium dialysis or equivalent assay). Thyroid imaging (scanning) with pertechnetate (^{99m}Tc) is also a very useful diagnostic aid in the evaluation of hyperthyroidism in cats because it delineates functioning thyroid tissue. With pertechnetate thyroid scanning, a one-to-one ratio usually exists between the size and intensity of the salivary glands and the two thyroid lobes. In contrast, most cats with hyperthyroidism will have obvious enlargement of one or both thyroid lobes, together with an increased uptake of pertechnetate into the abnormal thyroid tissue, as compared to the salivary glands. Calculation of the percentage thyroidal ^{99m}Tc uptake can also be determined for additional diagnostic value. Another major usefulness of thyroid imaging, however, is in determining the extent of thyroid gland involvement and in detecting possible metastasis.

The treatment of choice for an individual hyperthyroid cat depends on several factors, including the age of the cat, presence of other major medical problems, availability of a skilled surgeon or I-131 facility, and owner's opinion and financial options. Of the 3 forms of treatment available, only surgery and radioactive iodine remove and destroy the adenomatous thyroid

tissue, respectively, and thereby "cure" the hyperthyroid state. Use of an antithyroid drug (e.g., methimazole or carbimazole) will block thyroid hormone synthesis; however, since antithyroid drugs do not destroy adenomatous thyroid tissue, the nodule is not destroyed and will continue to grow in size. In some cats, benign thyroid adenoma or adenomatous hyperplasia appears to transform into thyroid carcinoma, especially after long-term treatment with antithyroid drugs.

Euthyroid Goiter in Cats

Experienced veterinarians can palpate ventral cervical nodules(s) in many middle-aged to older cats. It is not uncommon in 2010 to palpate a cervical nodule in a cat with no clinical or laboratory signs of hyperthyroidism. Possible differential diagnoses include early hyperthyroidism, thyroid cyst or cystadenoma, or non-functional thyroid adenoma or carcinoma. Nonfunctional thyroid carcinoma does occur but is rare in the cat. If an obvious cervical nodule is palpated in a cat with a normal T4 concentration, a fine needle aspirate should be considered to determine the tissue of origin. Thyroid imaging is again a very useful diagnostic aid in these cats and is considered by most to be the most sensitive means of diagnosis of early preclinical hyperthyroidism. In most of these cats, medical therapy is not indicated until clinical or biochemical hyperthyroidism develops.

Thyroid Cysts in Cats

Reports of cystic thyroid masses in cats are not uncommon, usually developing in cats with overt hyperthyroidism. Some of these masses may rapidly increase in size and rarely, signs related to local compression of adjacent structures (e.g., trachea) may develop in some cats. Diagnosis is based on palpation of the fluctuant mass, documentation of the cystic lesion with ultrasound, and aspirating the cystic fluid (which is typically serosanguinous). One can also determine T4 levels in the fluid to help confirm that the cystic lesion is of thyroid origin. Thyroid imaging can also be very helpful in determining if the cystic mass is of thyroid origin.

Treatment with either surgical excision or radioiodine has proven most successful in these cats. Long-term medical treatment of these cases is not recommended since the cystic lesions may increase greatly in size over time.

Congenital Hypothyroidism in Cats and Dogs

In dogs and cats, there are 2 major causes for congenital primary hypothyroidism: 1) thyroid dysmorphogenesis (defect in the biosynthesis of thyroid hormones); and 2) thyroid hypo- or aplasia. With thyroid dysmorphogenesis, the loss of T4's negative feedback effect on the pituitary leads to increased secretion of TSH, with resultant stimulation and hyperplasia of

the thyroid gland. This can lead to an enlarged thyroid gland (goiter). In contrast, the thyroid would be small in animals with thyroid hypo- or aplasia.

Thyroid hormones are essential for normal post-natal development of the skeletal and nervous systems. Therefore, congenital hypothyroidism is characterized by disproportionate dwarfism and neurologic abnormalities. Obviously many signs observed in adult-onset hypothyroidism can also be present in affected puppies and kittens. On physical examination, hypothermia, bradycardia and palpable goiter may be present in those animals with thyroid dysmorphogenesis.

In young dogs and cats with suspected congenital hypothyroidism, thyroid scintigraphy can be a useful diagnostic aid since the thyroid image differs depending on the cause. With thyroid dysmorphogenesis (hypo- or aplasia), no thyroid uptake is seen, whereas the thyroid lobes have a normal to increased size with normal to increase uptake in dogs and cats with thyroid dysmorphogenesis.

Treatment for congenital hypothyroidism consists of L-T₄ supplementation; with therapy, the goiter will decrease in size as the circulating TSH concentration falls into the reference range. For congenital hypothyroidism, prognosis is rather guarded and will largely depend on the underlying etiology of the hypothyroidism and age at diagnosis.

Thyroiditis in Dogs

Autoimmune or lymphocytic thyroiditis is the main pathologic process causing hypothyroidism as an adult-onset condition in dogs. It is well known that at least 50% of primary hypothyroidism in dogs result from immune-mediated thyroiditis. Rarely, early in the course of the inflammatory process, palpable enlargement of the thyroid gland is possible in some of these dogs. As thyroiditis progresses, parenchyma is destroyed and replaced by fibrous connective tissue and the goiter resolves. Diagnosis of hypothyroidism and thyroiditis is based upon measurement of serum T₄, cTSH, and thyroglobulin autoantibodies. Some of these dogs with thyroiditis will develop autoantibodies to T₄, T₃, or both. These autoantibodies produce spurious results when serum or plasma T₄ or T₃ are measured by radioimmunoassay, often resulting in an elevated apparent concentration of the thyroid hormones in affected dogs. Not uncommonly, these values will be markedly increased, causing the veterinarian to consider the possibility that the dog has hyperthyroidism due to thyroid neoplasia. The differentiation between hyperthyroidism and clinical hypothyroidism (due to thyroiditis) can usually be made on a clinical basis, as well as by measuring free T₄ concentrations (which typically are low in this situation). If hypothyroidism is present in these dogs with lymphocytic thyroiditis, treatment with L-T₄ supplementation is indicated.

Thyroid Tumors in Dogs

In dogs, thyroid tumors are common, representing approximately 1 to 4% of all canine neoplasms. As opposed to the relatively small, non-invasive thyroid tumors (i.e., adenomatous hyperplasia) associated with hyperthyroidism in cats, most clinically detected thyroid tumors in dogs are large, invasive carcinomas that are not hyperfunctional (i.e., do not produce hyperthyroidism). Most thyroid carcinomas in dogs arise from follicular cells, although up to a third of thyroid tumors may arise from parafollicular (C-cells), resulting in medullar C-cell carcinomas. Thyroid follicular carcinomas can be further subclassified as follicular, compact, compact-follicular (mixed), papillary, or undifferentiated, depending on the pattern of growth. Most canine thyroid tumors are mixed compact-follicular, whereas pure follicular or compact tumors or undifferentiated tumors are less common. Papillary carcinoma, a common tumor type in human patients, is very rare in dogs. Unfortunately, histological differentiation of these thyroid tumor types is generally of little help clinically when deciding on the best treatment for these carcinomas. In dogs with thyroid carcinoma, both local invasion of tumor into adjacent and distant metastasis are common. Approximately 50% of dogs with thyroid carcinoma have metastasis at time of diagnosis. During the natural course of disease, 65-90% of dogs with untreated disease will develop metastasis.

Many dogs with thyroid tumors are presented because the owner has noticed an enlargement of the neck. In >75% of dogs diagnosed in 1 survey, either the cervical swelling was the only reason for seeking veterinary care or the thyroid mass was detected by the veterinarian during an examination for another problem. Unlike the relatively small, freely movable thyroid tumors of the cat, most thyroid tumors in dogs are very large, easily palpable, and are well-embedded (fixed) into the surrounding soft tissues of the neck.

Thyroid imaging (scanning) is useful in the evaluation of dogs with thyroid masses because the procedure delineates functioning thyroid tissue. ^{99m}Tc-pertechnetate (^{99m}Tc) thyroid scans do not provide direct information regarding thyroid function, but such imaging procedures do aid in demonstrating the location of abnormal thyroid tissue. Thyroid imaging can also be performed to help determine the extent of thyroid invasion or metastasis. Failure to identify distant metastatic sites with thyroid imaging, however, cannot prove that distant metastasis does not exist.

Treatment of thyroid neoplasia in dogs is dictated by the size of the primary tumor, extent of local tissue invasion, presence of detectable metastasis, presence of hyper- or hypothyroidism, and available options. Because most clinically detected thyroid tumors in the dog are malignant, treatment is rarely curative. Nevertheless, one should generally advise some form of treatment because palliative relief and increased lifespan can usually be achieved in most dogs with thyroid carcinoma. Surgery, chemotherapy, cobalt irradiation, and use of

radioactive iodine therapy, alone or in combination, may be indicated depending on the individual dog. Medical control of the hyperthyroid state can be achieved by the daily administration of an antithyroid drug such as methimazole or carbimazole (5 to 15 mg/dog, twice, daily), but such medical treatment will not do anything to prevent tumor growth or metastasis.

TABLE 1. DIFFERENTIAL DIAGNOSIS FOR CERVICAL NODULES/MASS IN DOGS AND CATS

Category	Subcategory	Typical Clinical Syndrome	Species Affected
Neoplastic Disorders of Thyroid	Euthyroid goiter	None	Cat
	Thyroid cysts/cystadenoma	Euthyroid or hyperthyroidism	Cat
	Thyroid adenomatous hyperplasia	Hyperthyroidism	Cat
	Thyroid adenoma	Hyperthyroidism	Cat
	Thyroid malignancy/carcinoma	Usually hyperthyroidism	Cat
	Thyroid carcinoma	Usually nonfunctional	Dog
	Thyroid medullary carcinoma	Usually nonfunctional	Dog, Cat
Immune-Medicated Disorders of Thyroid	Thyroiditis (Hashimoto's)	Hypothyroidism	Dog, Cat?
	Hashimoto's hyperthyroidism	Transient hyperthyroidism	Dog
Congenital Disorders of Thyroid	Congenital hypothyroidism	Hypothyroidism	Cat, Dog
	Juvenile hypothyroidism	Hypothyroidism	Cat, Dog
Endocrinopathies with Thyroid/Parathyroid Nodule	Acromegaly	Growth hormone excess; secondary thyroid enlargement	Cat, Dog

	Primary hyperparathyroidism	Hypercalcemia; parathyroid nodule palates like thyroid	Cat, Dog
Congenital Cysts in Cervical Region	Ultimobranchial cyst	None	Dog, Cat
	Thyroglossal cyst	None	Dog, Cat
	Branchial cyst	None	Dog, Cat
	Dermoid cyst	None	Dog, Cat
		None	Dog, Cat
Nonthyroidal Neoplastic Disorders	Lipoma/Liposarcoma	None	Dog, Cat
	Lymphosarcoma	None	Dog, Cat
	Inflammatory conditions (e.g., abscess, granuloma)	None	Dog, Cat
	Salivary mucoceles	None	Dog, Cat
Non-thyroid Neoplastic Disorders	Regional soft tissue sarcomas, lymphoma, metastatic oral tumors	None	Dog, Cat

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Keywords

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