A Case-Based Approach to Complicated Hyperthyroidism
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**Thyroid Cysts in Cats:** Thyroid cysts are infrequently observed and reported in cats. Until recently, there was only a handful of case reports in the literature that described clinical signs attributed to the size of the mass and association only with thyroid cystadenomas. Given the paucity of information, a multi-center retrospective study of thyroid cyst presenting to four referral hospitals over the period of ten years was undertaken.

The clinical presentation of thyroid cysts most often follows owner observation of ventral cervical mass or signs referable to the size of the thyroid cyst such as dyspnea, dysphagia, and/or weight loss. Physical examination often reveals a very large and fluctuant feeling ventral cervical mass. In the retrospective study the majority of the cats presented two years after diagnosis of hyperthyroidism, with only 3 cats have non-functional cystic thyroid tumors. No specific clinicopathological abnormalities were found associated with thyroid cysts. Thyroid fluid was most often red to brown and had evidence of inflammation or hemorrhage with only a few tumors being reported out as neoplastic. Thyroxine levels measure in thyroid cyst fluid did not correlate with serum thyroxine levels. Thyroid cysts were easily identifiable on cervical radiographs or cervical ultrasound. Thyroid scintigraphy most often revealed hyperfunctional thyroid masses with large photopenic thyroid cysts.

Twenty eight hyperthyroid cats with thyroid cysts were treated with radioiodine. Of these, half received $\leq 10$ mCi while half received $>10$ mCi. Hyperthyroidism resolved in 23/25 cats in which follow-up data was available. Ten cats became hypothyroid with the majority being cats that received $>10$ mCi of radioiodine. Thyroid cysts resolved with radioiodine alone in 12/24 cases in which outcomes were available. In small cysts, cysts resolved with both doses of radioiodine, whereas larger cysts appeared to resolve more frequently with $>10$ mCi of radioiodine, though sample sizes were insufficient for this finding to be statistically significant. Eight cats underwent surgical thyroid-cystectomy. Three cats had already been treated with radioiodine which failed to resolve the cystic component of their disease. Five cats (2 euthyroid, 3 hyperthyroid) underwent surgical thyroid-cystectomy as their primary therapy. In the five cats that had unilateral thyroid-cystectomy, the treatment was effective and did not result in significant complications. In three cats that underwent bilateral thyroid-cystectomy, severe iatrogenic hypocalcemic developed post-operatively which led to owner election of euthanasia in all three cases. Histopathology in these cases revealed equal numbers of thyroid carcinomas and cystadenomas.

In conclusion, thyroid cysts are rare, but may be seen in both hyperthyroid and euthyroid cats, but most often occurs following long standing hyperthyroidism. Large cysts more often lead to dyspnea and dysphagia. Some cysts resolved with RAIT while others required surgical resection. Bilateral thyroid-cystectomy carries a high risk of iatrogenic hypocalcemia for which the clinician should be prepared to manage.

**Chronic Kidney Disease and Hyperthyroidism:** Both CKD and Hyperthyroidism are diseases of the senior cat population and thus do not infrequently occur in the same
Hyperthyroidism is well known to mask CKD in cats by increasing GFR through RAAS activation, beta-adrenergic stimulation, and glomerulotubular feedback. Hyperthyroidism may make diagnosing CKD challenging only revealing its presence after restoration of a euthyroid state. The prevalence of azotemia pre-treatment for hyperthyroidism has been reported to be between 10-23%, while 15-49% of cats develop azotemia after therapy for hyperthyroidism. CKD can also at times make the diagnosis of hyperthyroidism challenging, by shifting protein binding to decrease total T4. A T4 in a cat with CKD that is in the upper half of the reference interval should raise suspicion and be assessed with the addition of a free T4 by equilibrium dialysis +/- TSH. Multiple biomarkers including GFR studies, USG, and SDMA have been investigated in attempt to distinguish hyperthyroid cats that will become azotemic with therapy with no success at this time.

Cats with concurrent CKD and hyperthyroidism should be treated as chronic beta-adrenergic stimulation and RAAS activation will worsen CKD over time. The goals in treating these patients is to achieve and maintain euthyroidism with careful attention paid to avoid iatrogenic hypothyroidism or mild hyperthyroidism. Cats with pre-existing CKD should be IRIS staged. IRIS stage 1 and 2 cats should have a trial with a reversible therapy before proceeding with a definitive therapy. IRIS stage 3 and 4 cats may need a lower and more gradual introduction to anti-thyroid medications and definitive treatment should be pursued with caution. Regardless of treatment modality, GFR will decrease and creatinine will increase within 4 weeks of restoration of euthyroidism.

Methimazole should be started at 1.25mg PO or TD SID, and slowly titrated upwards with a CBC, chemistry profile, and total T4 assessed every 2 weeks. Maintenance of euthyroidism for four weeks should be enough time to assess if and to what degree of azotemia will reveal itself. If radioiodine is pursued, the T4 should be monitored more frequently (every 2 weeks) to determine how far and how quickly the T4 is falling. Levothyroxine can be introduced if needed to restore euthyroidism. In cases where owners can’t or won’t monitor this often, levothyroxine can be instituted at the time of discharge but will need to be tapered off over time as it will continue to suppress TSH and normal thyroid tissue will remain dormant while this medication is being given. A dose of 75ug PO BID is recommended in cats. Owners of cats with or at risk for developing CKD should be warned of the possibility of long term medication in their pets, particularly if this was a major reason for pursuit of radioiodine treatment.

Interestingly, survival time is not affected if cats develop azotemia after treatment for hyperthyroidism, but are shortened if they were azotemic before treatment. Development of iatrogenic hypothyroidism is a risk factor for developing azotemia and has been associated with shorter survival times as well.

**Thyroid Storm:** Thyroid storm occurs with a rapid increase in thyroid hormone levels leading to activation of the sympathetic nervous system and altered tissue sensitivity to catecholamines. In addition, concurrent illness can enhance the cellular response to thyroid hormones. Precipitating events include destruction of thyroid tissue (surgery, RAIT, overly vigorous thyroid palpation), abrupt withdrawal of antithyroid medications, and stress and non-thyroidal illness (particularly infections).

Clinical signs in cats are those of severe hyperthyroidism (tachypnea, tachycardia,
murmur, arrhythmia, but often more severe including respiratory distress, crackles or dull lung sounds, neurologic abnormalities, cervical ventroflexion, profound muscle weakness, sudden blindness, hypertension, or sudden death. There is no definitive diagnostic test to definitively determine a thyroid storm.

Treatment has five aims: 1) reduce production of thyroid hormone, 2) prevent further secretion of thyroid hormone, 3) counteract peripheral effects of thyroid hormone, 4) provide systemic support, and 5) determine and eliminate any predisposing factors. This typically means initiating therapy with methimazole (5 mg PO, TD, or per rectum), atenolol (1 mg/kg PO q 12-24 hrs), supportive care, and a general work-up including CBC, chemistry profile, urinalysis, urine culture, retroviral testing, and imaging.

Veterinarians should be particularly aware of this possibility when withdrawing anti-thyroid medications in preparation for patients who will be undergoing radioiodine therap. An attached checklist can help identify patients at risk and any concerns should be discussed with the treating institution.

References:


