

MEDICAL MANAGEMENT OF UNRESECTABLE THYROID CARCINOMA IN A FEMALE SHIH TZU DOG

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SUMMARY

Blondie, a client-owned 4 year old spayed Shih Tzu female dog was presented to Angel Animal Hospital with a protruding mass in the ventral aspect of neck in mid-October, 2015. Fine needle aspirate (FNA) exhibited cytopathological entities, apparently of Thyroid origin. Thyroid hormone assay revealed the hypothyroid status. The growth had increased to more than 2-times the original size after about 5-6 weeks. Histopathological evaluation of the punch biopsy tissue sample established follicular thyroid gland carcinoma. The clinical endocrinologist's review highlighted the risk of uncontrollable hemorrhage from the abnormally increased vascularity of the neoplastic tissue mass and ruled out surgical intervention. The case was then referred to the veterinary oncologist for radiation therapy protocol. The patient responded well, and no recurrence was observed during the following 24 weeks period.

Key words: Dog, hypothyroid, radiation therapy, thyroid carcinoma

Most common of all thyroid tumors in the dog, malignant form of cancer - usually appearing on one side of the neck region - is locally invasive with only chance of metastasis to the regional lymph node (s) and/or certain ectopic tissues. Most patients remain euthyroid, but a few (<5% with functional follicular tissue) may turn hyperthyroid, and some (~15%) become hypothyroid following extensive necrobiotic degenerative changes in the follicular functional tissue (Morgan, 2008). Golden retriever, Boxer and Beagle breeds are at increased risk. Middle aged or older dogs (>5 years age) are most susceptible, irrespective of gender. Thyroid follicular carcinoma in dogs is a potentially aggressive malignancy, exhibiting a marked propensity to invade through the thyroid capsule and metastasize into the lungs parenchyma, even before involvement of the regional lymph nodes becomes evident. Occasionally, thyroid carcinoma may arise in ectopic thyroid tissue, right up to the thoracic inlet and base of the heart.

The clinical signs on presentation include a perceptible cervical growth, dyspnea, hoarse bark, dysphagia and debility. Restlessness, nervousness, and fecal and/or urinary inconsistency are the usual clinical manifestations of the relatively rare hyperthyroid state. Tentative diagnosis is primarily based on detection of a palpable tumor mass in the ventral aspect of neck region with occasional enlargement of the regional lymph node (s). Corroborative evidence is provided by a judicious choice of imaging techniques: plain radiography of the cervical soft tissue mass, CT or MRI for elucidation of the extent of neoplastic transformation, and thoracic radiography for establishing metastatic disease (Taeymans *et al.*, 2013). For definitive histopathological evidence, fine needle aspirate (FNA) is not the ideal

sampling procedure; surgical punch biopsies are often mandated in suspected thyroid follicular tissue tumor. Hormone assay generally reveals increased thyroid hormones: total serum T₄ (thyroxine), or free T₄ titer concurrent with low or low-normal TSH titer. Differential diagnosis involves systematic elimination of the non-thyroid neoplasia: lymphoma, regional soft tissue sarcoma (STS) and metastatic oral tumors. The treatment options include surgery, the method of choice (Klein *et al.*, 1995), radiation therapy (Brearley *et al.*, 1999; Pack *et al.*, 2001), radio isotope I¹³¹ therapy (Adams *et al.*, 1995; Worth *et al.*, 2005), or a judicious combination of these remedial strategies. The prognosis, depending on severity of the clinical episode, is variable (Theon *et al.*, 2000).

Blondie, a client-owned 4 year old spayed Shih Tzu female dog was presented to the Angel Animal Hospital, Farmington Hills, Michigan (USA) with a perceptible mass in the ventral aspect of neck. Periodic episodes of dullness, lethargy, and tendency to put on extra body weight in the face of anorexia were the main features of the case history. Fresh blood samples for thyroid hormone assay at the specified pre-and post-treatment intervals were tested at IDEXX Laboratories (USA). The initial (pre-treatment) hormone assay revealed total T₄ titer, 0.7 µg /L (reference range, 1-4 µg/L), corroborating the suspected hypothyroid state of the patient. The daily oral levothyroxine supplementation regimen effectively upgraded the thyroid status to near normal, 1 µg /L after 10 days. Moderately increased daily oral dose of levothyroxine boosted the thyroid status further; the value was raised to 1.4µg/L during the follow-up hormone assay after seven and half month. Demonstration of free blood/Hb (3+), red blood cells (> 100/HPF, 400x) and white blood cells (6-10/ HPF, 400x) in the free catch pre-treatment urine sample indicated the possibility of urinary

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Fig. 1. Blondie preparations for biopsy

tract infection (UTI). Blondie was, therefore, also given oral antibiotic therapy to clear off the suspected infection. The client was advised to keep the patient on normal diet and light exercise, and report back to the clinic for any SOS healthcare assistance. The hematological attributes remained within their respective reference range at the pre-treatment interval. Concurrent blood chemistry profile showed that whereas blood urea nitrogen (BUN) and serum creatinine values remained within the respective reference interval, the more sensitive parameter of renal endothelial dysfunction, symmetric dimethyl-arginine (SDMA) titer (18 $\mu\text{g/dL}$) was moderately elevated (reference range 0-14 $\mu\text{g/dL}$), pointing to possible early kidney disease. The marginally increased serum alanine aminotransferase (ALT) titer 124 U/L (reference range 18-121 U/L) did not appear to be clinically significant, and the hepatic function remained apparently normal. This contention is supported by the observation that serum bilirubin (total, conjugated and unconjugated) values, and also the total protein and fractions, albumin/globulin (A/G) ratio remained within the respective reference interval. The serum aspartate aminotransferase (AST) and creatine kinase (CK) titers had increased adversely above the respective normal reference range. However, restoration of the normal values of these clinical enzymes points to the structural patency of plasma membranes in the myocardium cells, post-treatment (Intervals I and II). The circulatory calcium and inorganic phosphorus concentrations and serum alkaline phosphatase (ALP) titer remained within the respective normal range, indicating the structural and functional integrity of long bones. Circulatory titers of electrolytes: sodium (Na^+), potassium (K^+), chloride (Cl^-) and bicarbonate (HCO_3^-), remaining within the respective reference range, attested to fluid-cum-electrolyte homeostasis. Further, the routine urinalysis showed no evidence of any metabolic abnormality. Taking stock of all the available evidences, it was decided to explore the feasibility of total surgical excision of the neoplastic mass in the ventral neck region

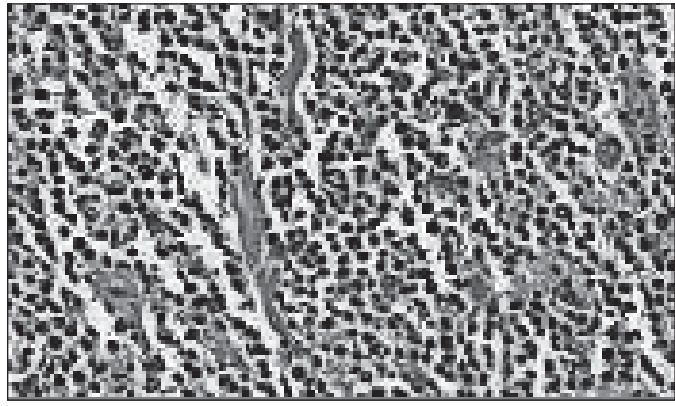


Fig. 2. Thyroid carcinoma degraded cells (HE. 400X)

of the patient, enlarged perceptibly to more than double the original size. Biopsy surgery was performed. In the atropinized patient, anesthesia was induced intravenously with propofol and maintained with isoflurane gas (Fig. 1).

In-house evaluation of FNA slides of the growth revealed the presence of a few neoplastic cells, presumably of thyroid origin. Histopathological review and identification of the neoplasm with suitably preserved punch biopsy tissue samples of the growth at IDEXX Laboratories revealed that the dense cellular mass with moderately thick fibrous tissue - formed by anatomizing cords and trabecule along with occasional acinar structures comprising closely adhering cells supported by a fine fibro-vascular stroma - was prone to infiltrative proliferation. Degraded cuboid or oval cells, mostly with indistinct borders and scanty eosinophilic cytoplasm, revealed signs of pleomorphism of mild to moderate intensity (Fig.2).

Some cells presented a finely granular and vacuolated appearance in the cytosolic compartment and centrally placed round nucleus with finely stippled chromatin, mostly with a single amphophilic nucleolus. In the remaining intact glandular structures, the cells contained eosinophilic debris of colloid consistency. The mitotic figures ($<1/10$ HPF, 400x), were rare. Though no classical evidence of vascular/ lymphatic invasiveness was forthcoming, yet in some focal areas the mass - still bound by an endothelial layer - exhibited signs of invagination into the luminary space of capillaries. Thus, the possible existence of an adjoining area of true vascular invasion could not be ruled out. The pathologist's interpretation of the characteristic histopathological features was right thyroid follicular carcinoma.

Further, consultation with the veterinary oncologist was recommended for staging of the malignant growth and suggesting the best remedial treatment. The oncologist totally ruled out surgery and recommended fractionated radiation therapy, readily accepted by the well-informed client. Upon completion of all procedural

documented modalities, the dog patient was treated in the nearby veterinary oncology clinic with 48 Gy during the treatment schedule of four consecutive weeks on every alternate day (total 12 exposures of 4 Gy/ fraction). The irradiation therapy was safe and effective with no detectable signs of local infiltration or metastasis. According to the pet owner's regular telephonic feedbacks, Blondie's behavioral pattern showed marked improvement, evidenced by playful disposition, free movements, and eating and sleeping well. No recurrence of growth was noticed in the follow-up visits at the clinic during the following 24 weeks period.

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