

Case report

A single report of skin disease associated with a functional thyroid carcinoma in a dog

機能性甲状腺癌に随伴して皮膚疾患を認めた犬に関する一症例報告

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Abstract: A 12-year-old neutered male Siberian husky dog was evaluated for alopecia, pyoderma, and diarrhoea suspected to be associated with a functional thyroid carcinoma. Treatment which included a thyroidectomy and subsequent thyroid supplementation led to the resolution of all associated clinical signs. There has been no recurrence of alopecia, pyoderma, or gastrointestinal abnormalities after one year of thyroid supplementation and post thyroidectomy. To the best of the authors' knowledge, this is the first report of a functional thyroid tumour in a dog associated with hair coat, skin, and gastrointestinal abnormalities.

Key words: canine, hyperthyroidism, endocrinology, dermatology, oncology

要約：12歳の去勢済、シベリアン・ハスキーに、機能性甲状腺癌に随伴すると考えられた脱毛、膿皮症および下痢が認められたため精査加療を行った。甲状腺摘出術と術後の甲状腺ホルモン補充療法により全ての臨床症状が消失した。また治療開始後1年の間、脱毛や膿皮症、消化器症状の再発などは認められなかった。著者らの知る限り、本論文は機能性甲状腺癌に随伴して被毛や皮膚、消化器に異常を認めた犬に関する初めての報告である。

キーワード：犬、甲状腺機能亢進症、内分泌疾患、皮膚疾患、腫瘍性疾患

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Introduction

Thyroid tumours represent 1.2% to 3.8% of all neoplastic disease affecting dogs^{2, 10}. Old dogs are predisposed with a median age of nine to eleven years affected^{2, 10}. Most thyroid carcinomas are non-functional. Sixty percent of affected dogs are euthyroid, 30% hypothyroid and only 10% are hyperthyroid². Clinical signs of hyperthyroidism include restlessness, polyphagia, weight loss, diarrhoea, and aggression^{2, 6, 10}. Cutaneous manifestations of hyperthyroidism associated with a functional thyroid tumour have not been

previously reported in dogs. In contrast, 36% of cats with hyperthyroidism exhibit excess hair coat shedding with unkempt and greasy hair coats⁶. This case report represents evidence of skin disease associated with a functional thyroid carcinoma in a dog.

Case report

A 12-year-old, 32.3 kg male, neutered, Siberian husky was referred for a three-month history of non-pruritic alopecia and recurrent bacterial pyoderma responsive to beta-lactamase antibiotics. The dog had chronic diarrhoea managed with probiotics and fibre supplements.

On presentation, the dog displayed signs of abnormal aggression. The temperature, pulse rate, and respiratory

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Fig. 1. Dull, unkempt hair coat with multifocal areas of alopecia.

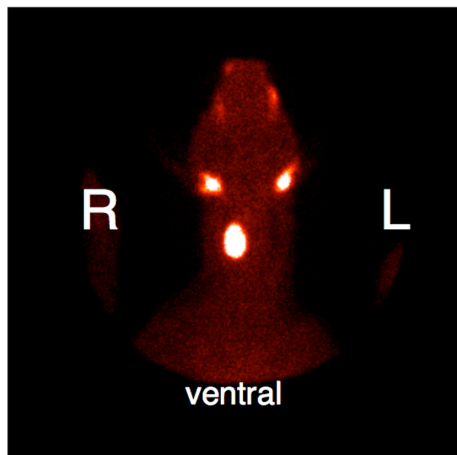


Fig. 2. Right thyroid lobe enlarged by a mass demonstrating markedly increased radionuclide uptake.

rate were within normal limits. Clinical examination revealed a dry, coarse hair coat in which the hairs epilated easily with associated patchy, multifocal, non-inflammatory areas of truncal alopecia (Fig. 1). Macroscopic examination of the alopecic lesions found fine, thinning hairs to complete alopecia. The skin surface was smooth with scarce, fine adherent scale. Multiple crusted and exudative lesions were evident affecting the trunk and limbs but were not seen in the alopecic areas. Muscle atrophy of the temporal muscles and hind limbs was noted.

Multiple superficial and deep skin scrapings and hair sampled for fungal culture using dermatophyte test medium (Hardy diagnostics; Santa Maria, CA, USA) were negative for mites and dermatophyte respectively. A trichogram was performed from the haired sample which only telogen hair shafts were present. Cytologic

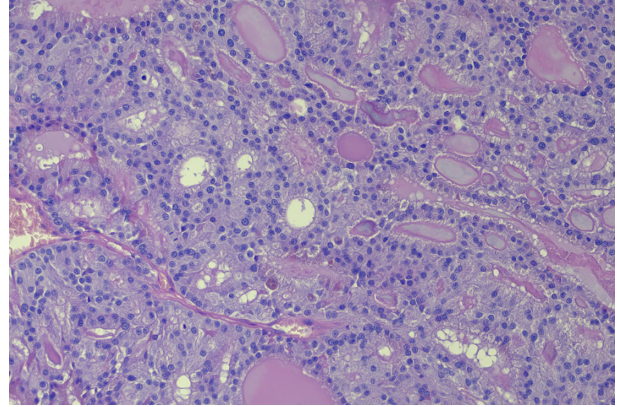


Fig. 3. Histopathology of thyroid carcinoma. An encapsulated, but locally infiltrative neoplasm composed of polygonal cells arranged in follicular structures containing colloid, as well as densely cellular, compact lobules and nests supported by a moderate amount of fibrovascular stroma.

evaluation of the lesional skin sites revealed neutrophils, macrophages, and numerous coccoid bacteria. A sterile swab from the affected skin surface was submitted for bacterial culture and sensitivity. The bacterial isolates were cultured using an agar based growth medium. Antimicrobial sensitivity was achieved by performing both a broth dilution method to identify the minimum inhibitory concentrations of the antimicrobials tested and a disk diffusion method to identify the zones of inhibition. The results revealed a methicillin sensitive *Staphylococcus pseudintermedius*. Cefpodoxime (Simplicef[®], Zoetis; Kundl, Austria) 6.2mg/kg daily for 28 days; topical daily 4% chlorhexidine spray (Trizchlor 4[®], Dechra; Overland Park, KS, USA) and twice a week bathing with a 4% chlorhexidine shampoo (Hexaderm[®], Vetbiotek; Largo, FL, USA) was commenced. A blood sample for evaluation of total triiodothyronine (T3), total thyroxine (T4), free thyroxine by equilibrium dialysis (FT4ED), endogenous canine thyroid stimulating hormone (cTSH), and T3 and T4 autoantibodies was submitted. A urine sample was submitted for routine urinalysis.

Elevations of total T3: 347 ng/dl (normal range, 45–150 ng/dl), total T4: 5.4 µg/dl (normal range, 0.8–3.5 µg/dl) and free T4 56.8 pmol/l (normal range, 8–40 pmol/l) were evident. The TSH value was <0.03 ng/dl (normal range, 0–0.60 ng/ml). T3 and T4 autoantibodies were both less than 2.0 µg/dl. Thyroid scintigraphy which consisted of an intravenous (IV) administration



Fig. 4. Hair coat one year post-operative adenocarcinoma thyroidectomy.

of a radionuclide followed by a series of static images was performed and revealed a 5cm diameter right-sided functional thyroid tumour (Fig. 2). A thyroidectomy was performed and the mass excised. Histopathologic evaluation confirmed the diagnosis of a thyroid carcinoma (Fig. 3). The owner elected not to pursue any adjunctive chemotherapy.

Post-operatively the dog was beginning to display signs of hypothyroidism which included lethargy and depression. Oral levothyroxine (Thyro-tabs[®], Lloyd; Shenandoah, IA, USA) at 0.3 mg (0.01 mg/kg) twice daily was commenced based on the clinical signs and the belief that it will inhibit tumour growth by suppressing TSH^{3, 7)}. After three and five weeks of supplementation, a post-pill T4 level at four hours after administration was 2.9 µg/dl and 1.7 µg/dl (normal reference range: 2.5–6.0 µg/dl) respectively. The antimicrobial therapy had successfully resolved the skin infection but the alopecic areas remained. Due to lack of hair growth, the levothyroxine dose was increased to 0.6 mg (0.02 mg/kg) twice daily. A post-pill T4 level repeated after three weeks of supplementation was 5.3 µg/dl. Hair growth was evident at this time, eight weeks after initially starting oral levothyroxine. After one year of appropriate supplementation the dog had a full, thick hair coat with no skin lesions and no recurrence of bacterial pyoderma (Fig. 2). The diarrhoea and abnormal stools had resolved. The post-pill T4 level was 5.2 µg/dl.

Discussion

To the author's knowledge this is the first reported case of skin disease with evidence supporting an association with a functional thyroid tumour in a dog. Previous reports in veterinary medicine are limited to three captive bred raccoon dogs (*Nyctereutes procyonoides*) from Japan with partial alopecia and scale associated with a follicular cell carcinoma of the thyroid⁹⁾. In humans, approximately 0.5% to 4.3% of patients with thyrotoxicosis and 15% of patients with severe Graves' ophthalmopathy have cutaneous symptoms; typically, non-pitting oedema and induration of the skin along with occasional raised, hyperpigmented, violaceous papules⁵⁾. Cutaneous manifestations of thyroid carcinomas in humans are rare and usually due to disseminated neoplastic disease¹⁾. In this case, it was believed that the changes to skin were due to the thyrotoxicosis caused by the functional thyroid carcinoma and not due to metastasis.

There was no recurrence of pyoderma seen after appropriate antimicrobial therapy and treatment of the underlying thyrotoxicosis. While evidence supports the pyoderma was due to the functional thyroid carcinoma, it is difficult to say whether it was directly due to the thyrotoxicosis induced by the tumour or the tumour itself causing immunosuppression. The alopecic areas, however, did not have evidence of infection and had not been traumatized as the dog was non-pruritic. The belief is that the alopecia seen in this dog was in association with thyrotoxicosis caused by the functional thyroid carcinoma.

One of the weaknesses in trying to correlate the skin changes as a manifestation of the thyrotoxicosis was not obtaining histopathology from the alopecic areas at initial presentation. It is believed that changes on histopathology would have likely showed a non-inflammatory alopecia which can be seen with both hypothyroidism and hyperthyroidism. Skin biopsies are generally non-diagnostic in cases where thyroid dysfunction is suspected. A trichogram was performed and revealed telogen hair shafts. Telogen effluvium has been documented in humans with hyperthyroidism and may be due to inducing faster hair follicle cycling¹¹⁾. While we cannot definitively prove a direct manifestation, the absence of other underlying causes as well as the response seen with appropriate treatments supports the skin changes were likely related to the

thyrotoxicosis caused by the functional thyroid tumour.

Thyroid supplementation was commenced post-operatively due to inducing hypothyroidism and to inhibit tumour growth. Thyroid cancer will express TSH receptor on the cell membrane and responds to TSH stimulation by increasing expression of thyroid-specific proteins and by increasing the rates of cell growth⁷⁾. It is believed that by suppressing TSH secretion it will decrease the rate of progression of thyroid tumour growth^{3,7)}. Based on this belief the post-pill T4 levels were maintained at the high end of the normal reference range to continue suppression of TSH secretion.

Up to 25% of humans with hyperthyroidism report mild to moderate diarrhoea with frequent bowel movements⁴⁾. Increased small intestinal transit times have been reported in canine experimental hyperthyroidism⁸⁾. It is feasible that the diarrhoea in this dog was related to the hyperthyroid state.

In conclusion, this is the first report of a functional thyroid tumour in a dog in which thyrotoxicosis was believed to have led to associated hair coat, skin, and gastrointestinal abnormalities. Clinical signs resolved with surgical removal of the tumour and thyroid supplementation.

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