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Case Report

Follicular-Compact-Cellular Carcinoma in the Thyroid Gland of a Dog

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Abstract: This case was determined accidentally in a 1.5-year-old, cross-breed male dog during a necropsy for an experimental study conducted in our laboratory, following a clinical examination as well as haematological, biochemical and urine analyses. The dog was clinically healthy. Haematological and biochemical parameters, except for a decrease in serum triiodothyronine (T_3), and urine analysis findings were within the reference range. A mass 3 x 4 x 3 cm in size and 22 g in weight that was observed in the thyroid gland located in the left cranioventral cervical region at the level of the larynx was investigated macroscopically and microscopically. The cut surface of the mass was lobulated, hyperaemic and haemorrhagic and had necrotic areas. In the microscopical examination, this mass was diagnosed as follicular-compact-cellular carcinoma due to the presence of many incomplete follicular structures without colloid in their lumens, a few follicles filled with colloid in their lumens and solid areas surrounded by a fine connective tissue formed by pleomorphic, neoplastic cells resembling thyroid follicular epithelial cells and showing mitotic activity.

Key Words: Thyroid gland, follicular-compact-cellular carcinoma, dog

Bir Köpeğin Tiroid Bezinde Folliküler-Kompakt-Hücresel Karsinoma

Özet: Bu olguya, deneysel bir çalışma sürecinde 1,5 yaşlı melez bir erkek köpekte hematolojik, biyokimyasal ve idrar analizleri ile klinik muayenesini takiben yapılan nekropsi esnasında tesadüfen rastlanılmıştır. Köpek klinik olarak sağlıklıydı. Serum triiodothyronine (T_3) düzeyindeki azalma dışında biyokimyasal ve hematolojik parametreler ile idrar analiz bulguları referans değerler arasındaydı. Boynun sol tarafında, kranioventral bölgede, larinks hizasında yer alan tiroid bezinde bulunan 3 x 4 x 3 cm boyutlarında 22 g ağırlığındaki bir kitle makroskobik ve mikroskobik olarak incelendi. Kitlenin kesit yüzeyi lobüllü olup, hiperemik, kanamalı ve nekrotik alanlara sahipti. Kitlenin mikroskobik muayenesinde, tiroid follikül epitel hücrelerine benzeyen pleomorfik özellikte mitotik aktivite gösteren neoplastik hücrelerden oluşmuş, lumenlerinde kolloid bulunmayan çok sayıda tam şekillenmemiş follikül oluşumları, lumenlerinde kolloid bulunan az sayıda folliküler yapılar ve ince bir fibröz doku ile çevrili neoplastik hücrelerden oluşan solid alanların görülmesi bu tömoral yapıya folliküler-kompakt-hücresel karsinom tanısı koydurmuştur.

Anahtar Sözcükler: Tiroid bezi, folliküler-kompakt-hücresel karsinom, köpek

Introduction

Tumours of the thyroid gland are encountered more often in dogs and cats than in other animal species, representing approximately 1-4% of all canine neoplasms and representing 10-15% of primary tumours located in the head and neck (1-6). Most thyroid tumours are derived from follicular thyroid cells. They are classified as benign (adenoma), malignant (carcinoma) and tumours of thyroid C cells (2-8). In addition, they are classified as epithelial, mesenchymal or mixed tumours (1). Benign thyroid adenomas, which are usually small nonfunctional masses, are clinically uncommon and identified at necropsy as incidental findings (9-12) while more than 90% of clinically detected thyroid tumours in dogs are carcinomas (4-6,10,13,14).

In Turkey, there have been some retrospective studies investigating tumours in dogs (15-17). To the authors' knowledge, except for a report (18) describing thyroid adenocarcinoma in an Irish setter, follicular-compact-cellular carcinoma has not been observed.

In the present paper, the findings of clinical, macroscopic, microscopic, haematologic, biochemical and urine analyses in a cross-breed male dog with follicular-compact-cellular carcinoma are reported.

Case Definition

This case was determined accidentally in a 1.5-year-old, cross-breed male dog during a necropsy for an experimental study conducted in our laboratory, following a clinical examination as well as haematologic, biochemical and urine analyses. The total white blood cell (WBC), red blood cell (RBC) and platelets (Plt), lymphocyte (LY), monocyte (MO) and granulocyte (GR) WBC counts, haemoglobin (Hgb), haematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), red blood cell distribution width (RDW), mean platelet volume (MPV) and platelet distribution width (PDW) were determined by an automated haematology cell counter (Beckman Coulter). Serum alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase (CK), lactate dehydrogenase (LDH) activities (Biolabo, France), and urea, creatinine, glucose, total protein, albumin, direct bilirubin, calcium (Ca), magnesium (Mg) and phosphorus (P) (Chema Diagnostica, Italy) levels were determined by Shimadzu-UV 1208 UV/VIS Spectrophotometer with commercial kits. The serum globulin concentration was calculated by subtracting the albumin value from the total protein value. The serum T_3, tetraiodothyronine (T_4), free T_3 (FT_3), free T_4 (FT_4) and thyroid stimulating hormone (TSH) were measured by kits with a detection limit of 0.2 ng/ml, 0.5 µg/dl, 0.2 pg/ml, 0.1 ng/dl and 0.011 µIU/ml, respectively, using the ACS:180 Automated Chemiluminescence System. The physical (colour, turbidity), chemical (pH, specific gravity, protein, glucose, ketones, bilirubin, blood, nitrite, haemoglobin, urobilinogen) and microscopic (WBC, RBC, epithelial cells, crystals, casts) analysis of urine was performed within 2 h by urine analyser (Iris-500).

Tissue samples taken from the tumour mass were fixed in 10% neutral buffered formalin, and embedded in paraffin, sectioned (5-6 µm), mounted on glass slides and the sections were stained with haemotoxylin and eosin and Masson's Trichrome.

Results and Discussion

The dog was clinically healthy. Body temperature was 38.3 °C, respiratory rate was 22/min and heart rate was 105/min. The urine sample was yellow. Urine pH was 6 and specific gravity was 1.025. In the urine sample, 1-2 leukocytes and erythrocytes per high power field and 0.1 EU/dl urobilinogen were detected while protein, glucose, blood, haemoglobin, bilirubin, nitrite and keton were not determined. All haematological and biochemical values except for a decrease in T_3 level were within the reference values (Table).

Table. Haematological and biochemical parameters of the dog.

WBC (x 10^3/µl)	6.30	FT3 (PG/ ml)	2.15
LY (x 10^3/µl)	2.33	AST (IU/l)	25.5
MO (x 10^3/µl)	0.61	ALT (IU/l)	23.5
GR (x 10^3/µl)	3.36	CK (IU/l)	227.1
RBC (x 10^6/µl)	6.96	LDH (IU/l)	502.1
Hgb (g /dl)	16.4	ALP (IU/l)	130.3
Hct (%)	46.7	Urea (mg/dl)	38.9
MCV (fl)	67.1	Creatinine (mg/dl)	1.48
MCH (pg)	23.6	Glucose (mg/dl)	75.3
MCHC (g /dl)	35.1	Albumin (g/dl)	2.81
RDW (%)	14.3	Globulin (g/dl)	3.04
Plt (x 10^3/µl)	420	Total protein (g/dl)	5.85
MPV (fl)	8.6	Bilirubin (mg/dl)	0.08
PDW (%)	16.3	Ca (mg/dl)	10.03
T_4 (µg/dl)	1.3	Mg (mg/dl)	2.75
FT_4 (ng/dl)	1.20	P (mg/dl)	5.01
T_3 (ng/ml)	0.46	TSH (µIU/ml)	0.03

At necropsy, a dark coloured, firm, elastic mass, 3 x 4 x 3 cm in size and weighing 22 g was observed in the thyroid gland located in the left cranioventral cervical region at the level of the larynx. The mass was freely movable under the skin. The cut surface of the mass was lobulated and hyperaemic and haemorrhagic and covered by necrotic areas (Figure 1).

Microscopically, the tumour cells were cuboidal to prismatic, polygonal and with fine granules, and pale eosinophilic cytoplasm. The tumour cells had round or ellipsoidal centrally located nuclei. The chromatin of the nuclei had a fine granular structure and the nuclei had an apparent single nucleolus. A few pleomorphic cells with large nuclei as well as a few mitotic figures were observed in some areas between single type tumour cells. Some of these tumour cells formed varying sized follicles the lumens of some of which were filled with colloid (Figure 2), and some others formed solid areas surrounded by fine connective tissue (Figure 3). There were also some incomplete follicles with no colloid (Figure 4). These tumour cells resembled follicular epithelial cells. In the stroma, large haemorrhagic areas, inflammatory cell infiltration, fibro-oedematous areas and the formation of metaplasic cartilage in some areas were observed (Figure 5). There were no pathological lesions or areas of metastasis in the sections of other organs.

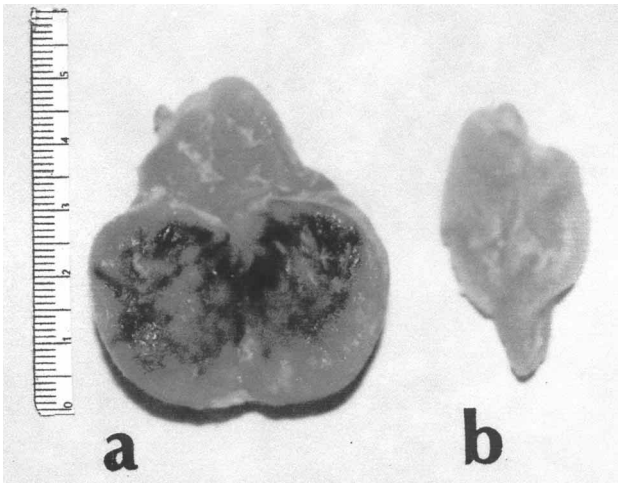

Figure 1. The cut surface of the thyroid gland with the tumour (a), the cut surface of a normal thyroid gland (b).

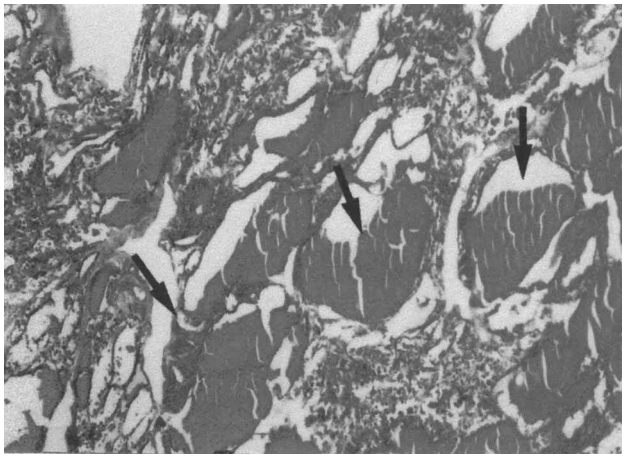

Figure 2. Follicles containing colloid in tumoural mass (arrows). Masson's Trichrome x 400.

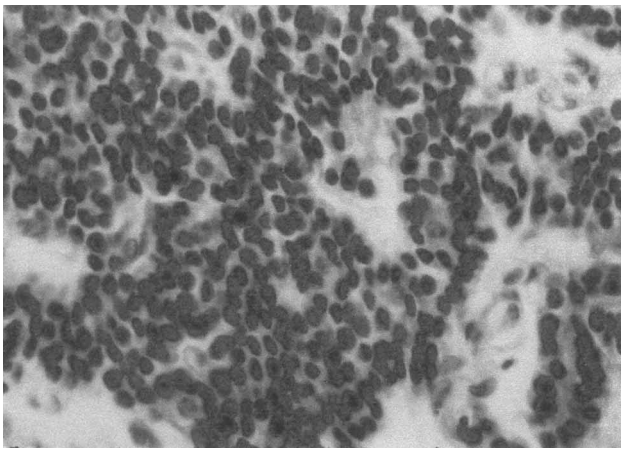

Figure 3. Solid areas formed by tumour cells. Masson's Trichrome x 400.

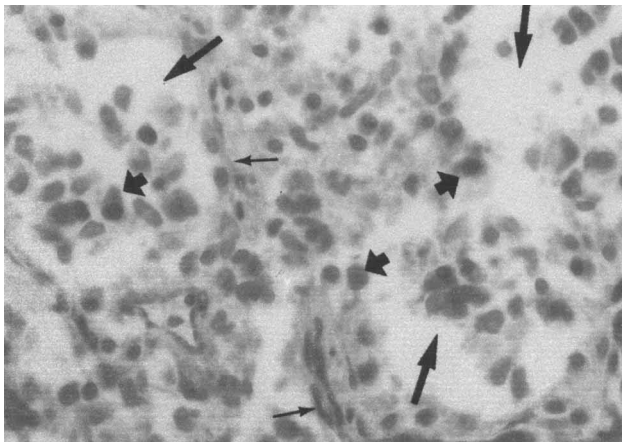

Figure 4. Incomplete follicles (large arrows), tumour cells (arrowheads), fine connective tissue (small arrows). H&E x 400.

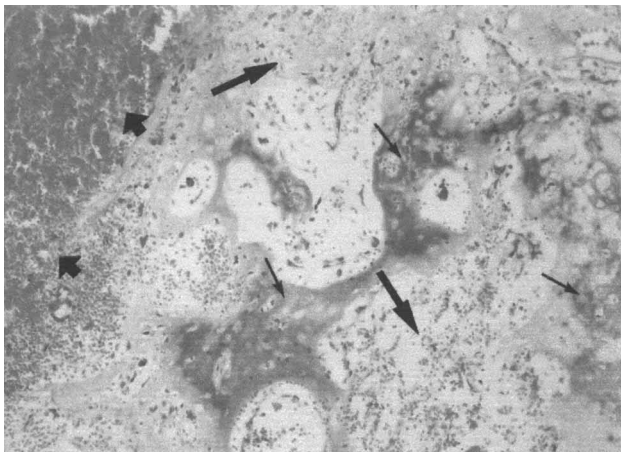

Figure 5. Haemorrhagic (arrowheads), inflammatory cell infiltration and oedematous areas (large arrows) and metaplasic cartilage formation (small arrows) in the tumour stroma. H&E x 200.

The localisation and macroscopic appearance of the mass was consistent with unilateral tumour cases reported in previous studies (1-3,9-12). Although immunocytochemical (19,20) and ultrastructural examinations (21) are useful for the differential diagnosis of tumours, in this case the diagnosis of the mass was performed by histopathological examination (1-3,7). Clinical, haematologic and biochemical findings were also evaluated to support the histopathology. As indicated in previous studies (2,3,7,17), microscopically this mass was diagnosed as follicular-compact-cellular carcinoma due to the presence of many incomplete follicular structures without colloid in the lumens, a few follicles filled with colloid in the lumens and solid areas surrounded by a fine connective tissue formed by pleomorphic, neoplastic cells resembling thyroid follicular epithelial cells and showing mitotic activity and large haemorrhagic areas, inflammatory cell infiltration, fibro-oedematous areas and metaplasic cartilage formation in the stroma.

Many studies (1-7) have suggested that dogs between the age of 5 and 15 years and boxers, beagles, golden retrievers and German shepherds are predisposed to tumours of the thyroid gland. However, in this case it is speculated that follicular-compact-cellular carcinoma is also seen in cross-breed and young dogs because of the observation of this type of tumour in a 1.5-year-old cross-breed dog.

Thyroid carcinomas in dogs are usually large, palpable and asymmetrical and local invasion of the tumour into adjoining structures such as the oesophagus, trachea, cervical muscles, nerves and thyroid vessels, and distant metastases such as pulmonary metastases are common (2,3,10,13,14). Because of the large volume of tumour masses and the high incidence of metastasis, clinical signs including dyspnea, cough, hoarseness, dysphagia, vomiting, anorexia and weight loss may be seen (4-6,9,14). Laboratory examinations of dogs with non-functional thyroid tumours show increases in ALT and ALP activities in 40% of cases, hypercalcaemia and a slight increase in plasma urea in less than 25%, and mild non-regenerative anaemia in 10% (5). However, in the present case, the haematologic and biochemical parameters and results of urine analysis were within the reference range, as indicated by Harari (12). The lack of the changes in haematologic and biochemical findings and metastases may explain the lack of clinical findings. Although most thyroid tumours do not secrete thyroid hormone into the circulation (4,9,10), in some thyroid tumour cases hypothyroidism or hyperthyroidism of up to 20% was reported (2,5,6,13). In this case, the levels of thyroid hormones were within the reference values except for the decrease in serum T_3 level.

In conclusion, macroscopic and microscopic findings showed that a tumour mass observed in a cross-breed male dog was follicular-compact-cellular carcinoma. During the necropsy, a detailed examination of the organs in the neck region would be valuable.

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