

Paratracheal Cervical Mass in a Dog

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Case Presentation

A 14-year-old female Welsh Terrier was presented for evaluation of multiple skin masses. The dog had been vaccinated routinely and given monthly heartworm prophylactic treatments and had no history of disease prior to presentation. The owner had noted the masses incidentally the previous day during bathing and clipping. On presentation the dog was in good body condition and alert. Results of clinical examination were unremarkable except for the presence of 2 cutaneous masses and 1 subcutaneous mass. Results of a CBC and serum biochemical profile were within reference intervals. Thoracic radiography was unremarkable.

One cutaneous mass was located on the dorsum and was diagnosed cytologically and histologically as a follicular (epidermal) cyst. The second cutaneous mass was located in the parotid gland region and was diagnosed cytologically and histologically as a sebaceous epithelioma. The subcutaneous mass was located in the cervical region. It was smooth, 2×3 cm (oval), well circumscribed, and loosely attached to the soft tissue adjacent to the left ventrolateral aspect of the cranial trachea.

A sample for cytologic examination of the cervical mass was obtained by fine-needle capillary sampling, in which a 25-ga 1-inch needle was inserted multiple times into the mass without aspiration. Smears were routinely prepared and stained with a quick Romanowsky-type stain (Hemacolor; Merck, Darmstadt, Germany) (Figure 1A and B).

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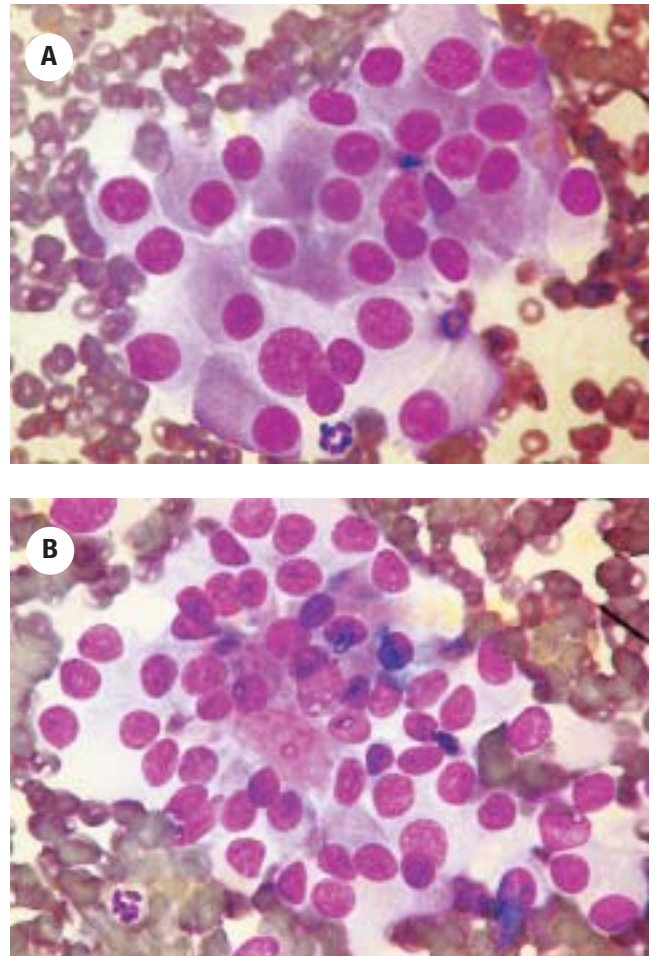


Figure 1. Fine-needle capillary sample from a paratracheal cervical mass in a dog (A,B). Hemacolor, ×100 objective.

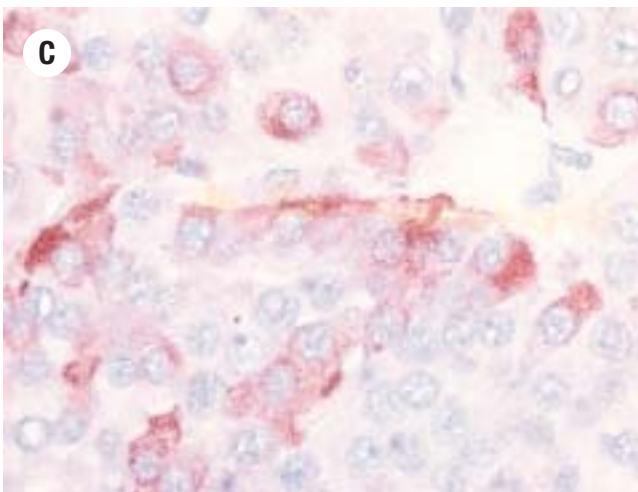
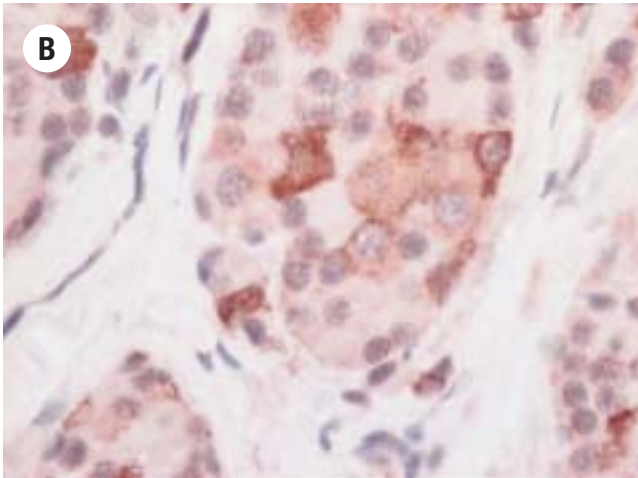
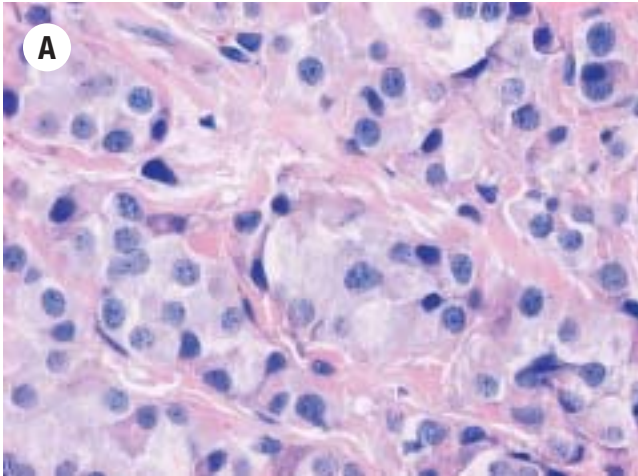


Figure 2. Histologic section of a medullary thyroid carcinoma in a dog. (A) Nests of densely packed polygonal cells with thin fibrovascular stroma. Hematoxylin and eosin, $\times 40$ objective. (B) Numerous neoplastic cells expressing cytoplasmic chromogranin A. ABC immunoperoxidase method, $\times 40$ objective. (C) Some neoplastic cells were positive for calcitonin in a cytoplasmic pattern. ABC immunoperoxidase method, $\times 40$ objective.

Cytologic Interpretation

The sample was moderately cellular and contaminated with blood. A single cell population was arranged in numerous clusters of variable sizes. Cells forming small clusters were arranged in a monolayer, whereas in larger clusters they were often superimposed. An acinar pattern was sometimes evident. Most cells ranged from 15-30 μm in diameter, but occasionally they were up to 40 μm . Cells were round to polygonal, with distinct cell borders and mild to moderate anisocytosis. Nuclei were round to oval and eccentric, with reticular to coarse chromatin and prominent nucleoli. Anisokaryosis was moderate to marked. Rare binucleated and multinucleated cells were observed. Nuclear pseudoinclusions were rarely seen. Cytoplasm was scarce to abundant, finely granular, and eosinophilic (Figure 1A). Rarely, multiple intracytoplasmic vacuoles were seen in some cells. Extracellular amorphous pink material was occasionally observed in some clusters (Figure 1B).

Differential cytologic diagnoses included neuroendocrine or endocrine tumors such as thyroid adenocarcinoma, C-cell or medullary thyroid carcinoma, carotid body chemodectoma, and parathyroid carcinoma. The eosinophilic pink extracellular material was consistent with colloid or amyloid, suggesting thyroid as the origin of the tumor. Medullary thyroid carcinoma was considered the most likely cytologic diagnosis. Thyroid adenocarcinoma was considered less likely because of the absence of intracellular dark blue granulation usually associated with follicular cells.

Gross Appearance and Histologic Interpretation

The left thyroid lobe was replaced by an oval tan 1 \times 2 \times 3-cm mass. The mass was well circumscribed and loosely adherent to the trachea and surrounding structures and thus was easily removed surgically. On cut surface, the mass was homogeneous.

Histologically, a nodular 1 \times 2-cm mass composed of rows and nests of densely packed cells separated by thin fibrovascular stroma was recognizable within the thyroid capsule (Figure 2A). Neoplastic cells were large, with indistinct cell borders and moderate to large amounts of pale eosinophilic dusty or finely vacuolated cytoplasm, occasionally containing small eosinophilic droplets of amorphous material. Nuclei were round to oval (14-20 μm in diameter) with finely dispersed chromatin and 1 or 2 darkly basophilic small nucleoli and occasionally contained large pseudoinclusions. Less than 1 mitotic figure was observed per high-power field ($\times 40$ objective). Scattered follicular structures containing homogenous eosinophilic amorphous material were entrapped among the neoplastic cells. Staining identi-

fied the amorphous material as colloid: positive for both thyroglobulin (rabbit polyclonal, Dako, Glöstrup, Germany, 1:4000 dilution) and the periodic acid-Schiff (PAS) reaction and Alcian blue-negative. Multiple cystic structures containing very pale eosinophilic amorphous material and lined with small cuboidal to flattened cells also were observed. This pale amorphous material was mucin, based on staining that was negative for thyroglobulin (rabbit polyclonal, Dako, 1:4000 dilution), positive with Alcian blue, and slightly positive for the PAS reaction. Hemosiderophages and scattered foci of hemorrhage and coagulative necrosis also were visible. A peripheral focus of sparsely cellular fibrous tissue with abundant amorphous extracellular substance (Congo red-negative, interpreted as hyalinized collagen) was seen.

Immunohistochemistry was performed to detect cytokeratin (mouse monoclonal, clone AE1/AE3, Zymed, South San Francisco, CA, USA), thyroglobulin (rabbit polyclonal, Dako, 1:4000 dilution), chromogranin A (rabbit polyclonal, Dako, 1:1000), calcitonin (rabbit polyclonal, Dako, 1:4000), and neuron-specific enolase (NSE; rabbit polyclonal, Dako, prediluted) by the avidin-biotin-peroxidase complex (ABC) method. Immunohistochemical results confirmed the C-cell origin of neoplastic cells: about 30% of neoplastic cells were positive for chromogranin A (Figure 2B), 40-50% were positive for calcitonin (Figure 2C), and about 80% were positive for NSE (not shown). Neoplastic cells were negative for cytokeratin and thyroglobulin. Based on histologic and immunohistochemical evaluation, a diagnosis of medullary thyroid carcinoma was made.

Discussion

Primary malignant tumors of the thyroid gland include neoplasia of follicular cell origin (thyroid adenocarcinoma) and parafollicular or C-cell origin (medullary thyroid carcinoma).¹ In both humans and dogs, the distinction between the 2 types of thyroid tumors is important because they have different prognoses.¹ Contrary to human tumors, canine medullary thyroid carcinomas are usually more encapsulated and less invasive than thyroid adenocarcinomas and carry a more favorable prognosis.¹ Malignant behavior and distant metastases can nevertheless occur in dogs with medullary thyroid carcinoma.² The tumor in this dog was well-encapsulated and easily resected. There was no clinical or radiographic evidence of metastasis, although extensive diagnostic imaging was not performed.

The paratracheal location of a cervical mass with the cytologic appearance of an endocrine or neuroendocrine tumor is consistent with a tumor of thyroid or parathyroid origin. Carotid body chemodectoma was consid-

ered initially as another differential diagnosis. However, this rare tumor usually arises near the angle of the jaw.³ Serum biochemistry results can aid in the differentiation between parathyroid adenocarcinoma and medullary thyroid carcinoma. Parathyroid adenocarcinoma may be associated with hypercalcemia.⁴ Although hypocalcemia can be found in some dogs with C-cell carcinoma,^{2,5,6} in a series of 12 dogs with medullary thyroid carcinoma, none had hypocalcemia, nor did the dog in this case.¹

Among canine thyroid tumors, the incidence of medullary thyroid carcinoma varies widely. In a series of 141 canine thyroid tumors, only 2 (1.4%) were classified as medullary thyroid carcinoma.⁶ In another retrospective study of 38 cases of canine thyroid neoplasms, 36% were considered to be of C-cell origin based on both histology and immunohistochemistry.¹ This discrepancy could reflect the difficulty in differentiating C-cell thyroid carcinoma from the more common thyroid adenocarcinoma histologically.¹ Immunohistochemistry is considered essential by some authors for distinguishing between these tumors.^{1,7} Medullary thyroid carcinoma is positive for chromogranin A and calcitonin, whereas thyroid adenocarcinoma is negative for these markers.⁷⁻⁹ The positive staining for calcitonin was useful in ruling out aortic body chemodectoma and parathyroid gland tumor in the dog of this report.⁸ Thyroid transcription factor 1 (TTF-1) is a new marker that has been recently studied in canine thyroid tumors.¹⁰ This marker has slightly lower sensitivity than thyroglobulin for detecting thyroid follicular tumors and lower sensitivity than calcitonin for detecting C-cell tumors.¹⁰ When used in conjunction with thyroglobulin staining, however, TTF-1 staining can increase the sensitivity for detecting follicular carcinomas.¹⁰

Amyloid is commonly found in the fibrovascular stroma of medullary thyroid carcinoma.⁷ Congo red staining failed to demonstrate amyloid in the tumor of this dog. Therefore, the pink extracellular amorphous material seen in the cytologic preparation was more likely colloid that may have been incidentally obtained from residual thyroid follicles during sampling. ◊

Abstract

A 14-year-old female Welsh Terrier was presented for evaluation of multiple skin masses. Two of them were diagnosed as a follicular (epidermal) cyst and a sebaceous epithelioma by cytology and histopathology. The third mass was located in the subcutis adjacent to the cervical trachea. Clinical findings, thoracic radiography, and laboratory results were otherwise unremarkable. Cytologically, the cervical mass was characterized by the presence of round to polygonal cells with distinct cell

borders, mild to moderate anisocytosis, round to oval eccentric nuclei with prominent nucleoli, and a variable amount of finely granular, eosinophilic cytoplasm. Differential diagnoses included endocrine/neuroendocrine tumors such as thyroid adenocarcinoma, medullary thyroid carcinoma, carotid body chemodectoma, and parathyroid carcinoma. The mass was removed surgically and submitted for histopathologic and immunohistochemical examination. Histologically, the mass was composed of rows and nests of densely packed cells separated by thin fibrovascular stroma. Neoplastic cells had moderate to large amounts of pale eosinophilic dusty or finely vacuolated cytoplasm and round to oval nuclei with finely dispersed chromatin and 1 or 2 small nucleoli. On immunohistochemistry, neoplastic cells were positive for chromogranin A, calcitonin, and neuron-

specific enolase, and were negative for cytokeratin and thyroglobulin. The final diagnosis was medullary thyroid carcinoma, an uncommon endocrine tumor of dogs that has cytologic and histopathologic features similar to other endocrine and neuroendocrine tumors. Immunohistochemistry or immunocytochemistry should be performed to differentiate medullary thyroid carcinoma from other endocrine/neuroendocrine tumors of dogs. (Bertazzolo W, Giudice C, Dell'Orco M, Caniatti M. Paratracheal cervical mass in a dog [medullary thyroid carcinoma]. *Vet Clin Pathol*. 2003;32:209-212)

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Key Words: C-cell thyroid carcinoma, cytology, dog, medullary thyroid carcinoma

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