Mediastinal mass in a dog.

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Signalment: Mixed-breed canine, 6 year old spayed female named Victoria

Specimen: Cytologic sample from mediastinal mass near the heart base.

History: Victoria was referred to the Oklahoma State University Boren Veterinary Medical Teaching Hospital (OSU-BVMTH) with a 6 month history of anorexia and lethargy. Four months previously the referring veterinarian documented icterus with moderately increased serum activity of ALT and ALP. Leptospirosis serology was negative, and the dog was treated empirically with antibiotics and fluid therapy. The icterus resolved and liver enzyme values improved, but were still increased. A pleural effusion was determined to be a modified transudate.

Clinical findings: Physical examination at OSU-BVMTH revealed a thin, lethargic dog with muffled heart sounds, jugular distension and jugular pulses. A CBC was unremarkable with the exception of lymphopenia. Liver enzymes were slightly increased: ALT 469 IU/L (RI 12 – 118), ALP 314 IU/L (RI 5 – 131), GGT 16 IU/L (RI 1 – 12). Total Bilirubin was increased at 13.7 µmol/L (RI 1.7 – 5.1). RI means reference interval. Thoracic ultrasound demonstrated a mediastinal mass surrounding the aorta at the base of the heart. Pericardial effusion was present and pericardiocentesis retrieved 0.4L of serosanguinous fluid. Radiographs showed multiple small nodules in both right and left lung fields and blunt liver margins. A fine needle aspirate of the heart-base mass was obtained and submitted to the OSU-BVMTH clinical pathology laboratory (Antech Diagnostics) for cytologic evaluation (Figures 1-4).

Questions:

1. What are the differential diagnoses for canine heart-base tumors?
2. Is histopathology alone sufficient to differentiate these tumors?
3. How can immunohistochemistry (IHC) be used to facilitate diagnosis?

Cytology of canine heart-base mass:

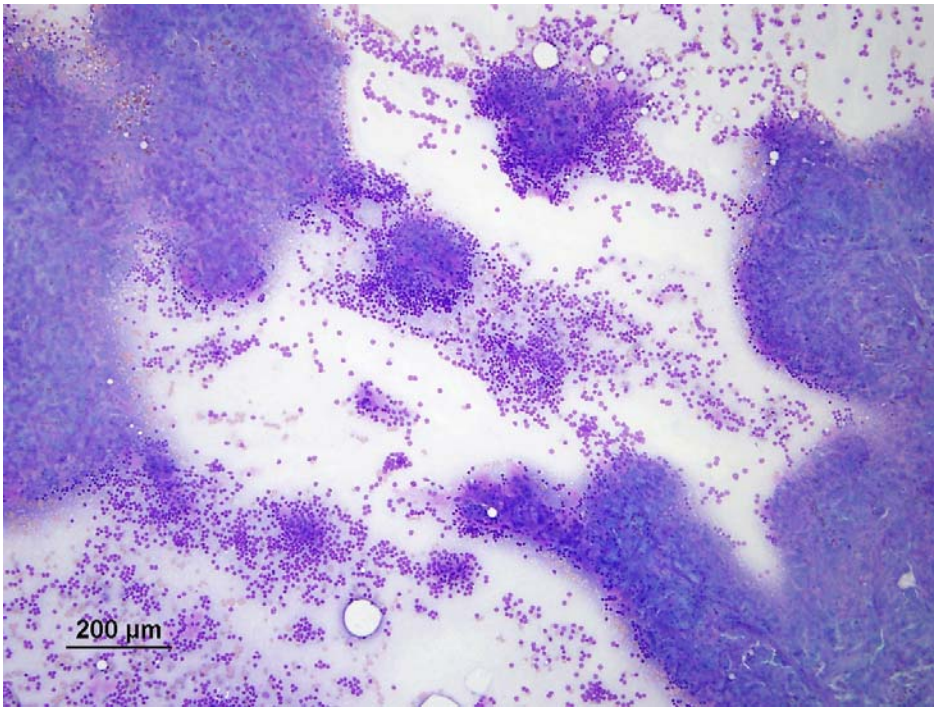

Figure 1. Aspirate of canine heart-base mass, X100 magnification, aqueous Romanowsky stain.

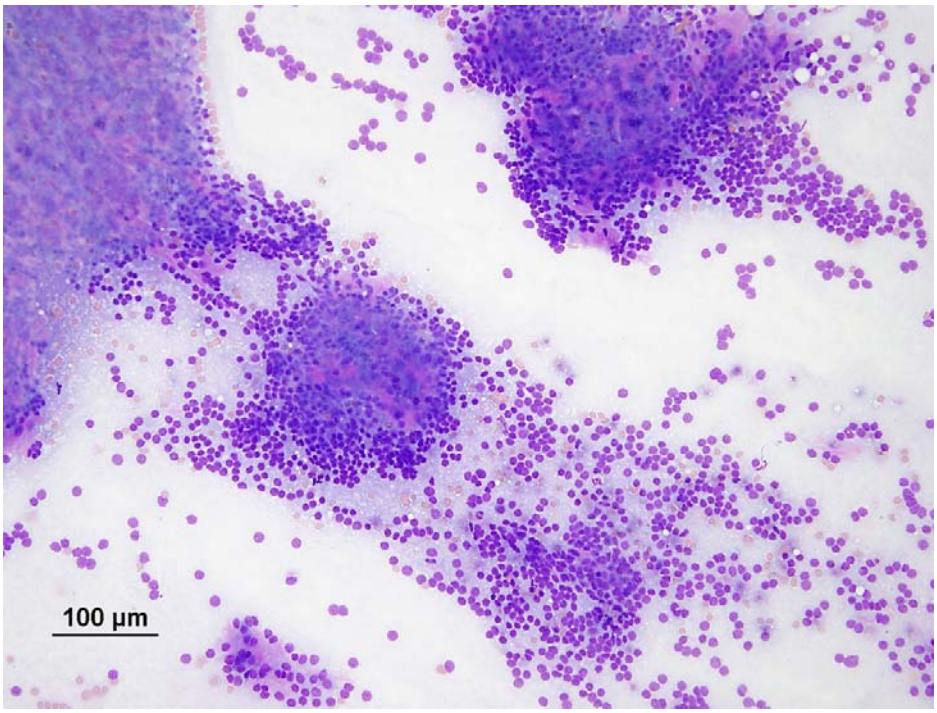

Figure 2. Aspirate of canine heart-base mass, X200 magnification, aqueous Romanowsky stain.

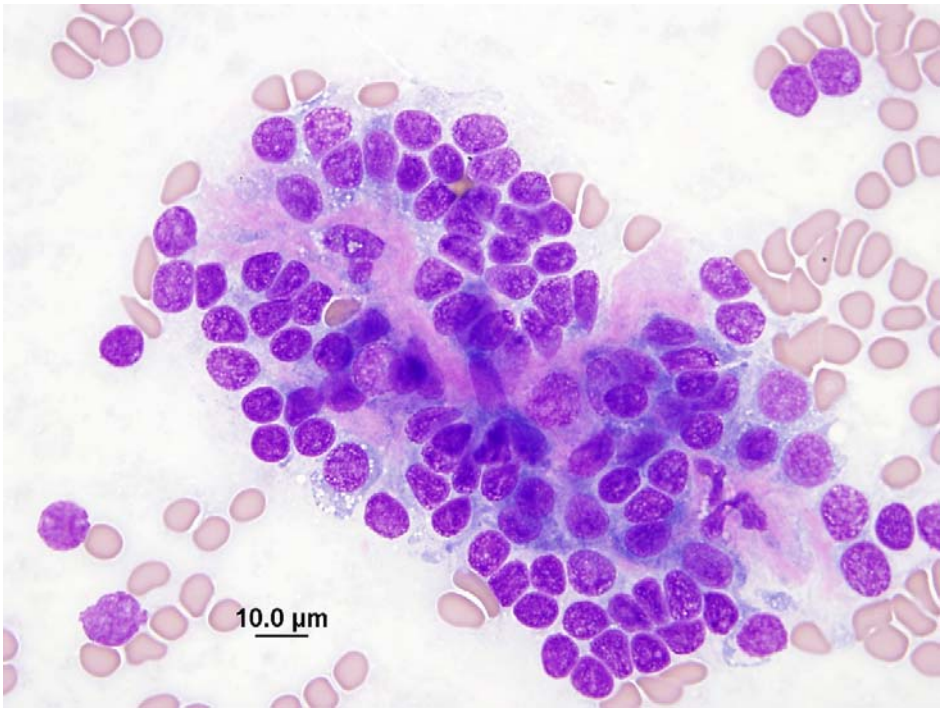

Figure 3. Aspirate of canine heart-base mass, X1000 magnification, aqueous Romanowsky stain.

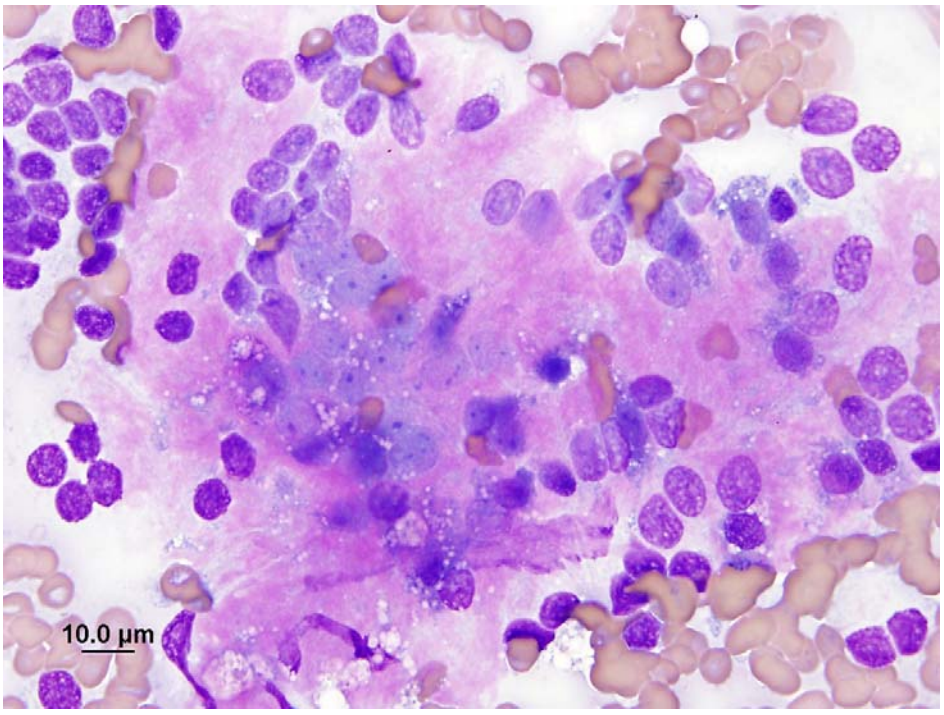

Figure 4. Aspirate of canine heart-base mass, X1000 magnification, aqueous Romanowsky stain.

Cytology interpretation: Probable ectopic thyroid tumor; possible chemodectoma

Cytology description and comments: The slides are highly cellular, containing large numbers of nucleated cells present individually and in variably-sized clusters in a background of abundant blood. Individualized cells are predominantly lysed, appearing as naked intact nuclei. Cells within clusters have uniform round to oval nuclei with granular chromatin and small indistinct nucleoli. Cytoplasm of intact cells is lightly basophilic and occasionally contains small clear vacuoles. Cellular pleomorphism is minimal, with slight anisocytosis and anisokaryosis observed. Throughout the slides there is a variable amount of eosinophilic extracellular material present. Cells are frequently surrounded by or embedded within this material, which is occasionally abundant within large cellular clusters.

The cells present have features consistent with endocrine/neuroendocrine origin. Although the location is typical for chemodectoma, the abundant extracellular material is suggestive of colloid, making ectopic thyroid tumor more likely in this case. Absence of cellular pleomorphism does not rule out malignancy in either case. Recommend biopsy and histopathology.

Clinical follow-up: A thoracotomy and subtotal pericardectomy was performed, and biopsies of the heart base mass and lung were obtained and submitted for histopathology. Victoria recovered poorly from anesthesia. Despite intensive support she developed anuric renal failure and was euthanized two days post-operatively. A necropsy was performed.

Necropsy and histopathology: There was a 12 x 9 x 7 cm multinodular soft tissue mass present at the base of the heart and partially invading the adjacent pericardium, extending cranially within the mediastinum to surround the aorta. Microscopically, the mass was expansile, unencapsulated and poorly demarcated with areas of necrosis and hemorrhage. Neoplastic cells were round to polygonal containing a central round nucleus with stippled chromatin and granular lightly eosinophilic cytoplasm. Neoplastic cells were often packeted within a fibrovascular stroma and were interpreted as neuroendocrine in origin (Figure 5).

All lung lobes contained numerous 4 – 6 mm diameter firm round nodules. Microscopically, these nodules contained packets of neoplastic cells similar to those observed in the heart base mass.

Disseminated throughout the liver and effacing greater than 60% of the parenchyma were numerous multinodular pale soft tissue masses. Microscopically, extensive regions of the liver showed near complete collapse of normal architecture, abundant hemorrhage, and replacement by fibrous connective tissue. Numerous nodules are composed of cords of regenerating hepatocytes. No neoplastic cells were identified in the liver. Changes were interpreted as consistent with an unknown previous hepatic insult.

Histopathologic diagnosis (initial): Neuroendocrine carcinoma (chemodectoma/aortic body tumor, presumptive) with pulmonary metastasis.

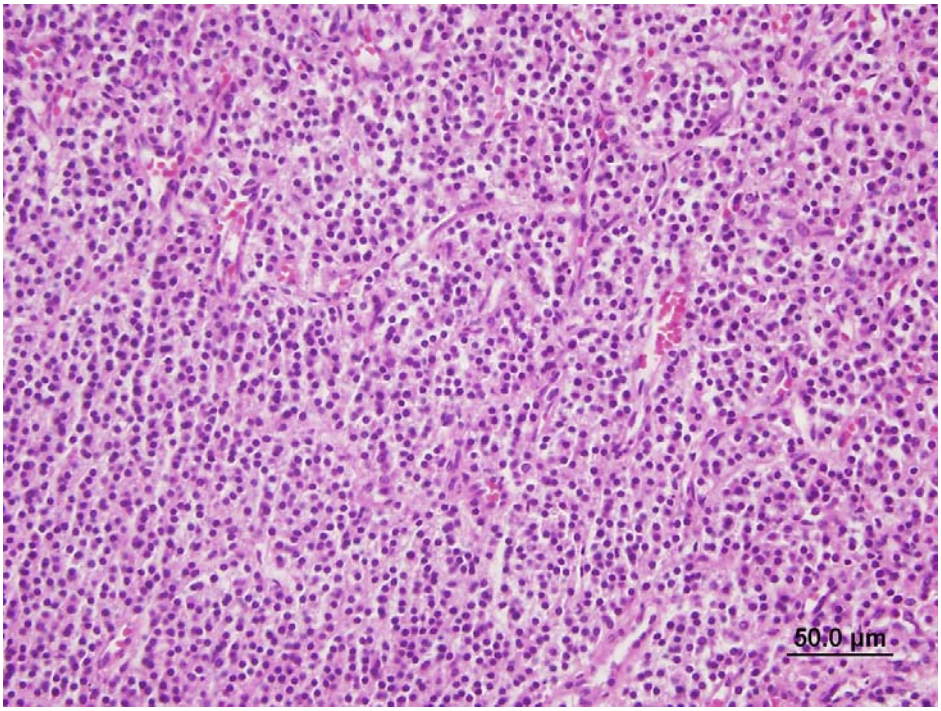

Figure 5. Histologic section of canine heart-base tumor, X400 magnification, H&E.

Additional tests: Immunohistochemistry (IHC) was performed to confirm the morphologic diagnosis of chemodectoma (Figures 6 – 7). Results are summarized in Table 1.

Table 1. Summary of IHC performed on canine heart-base tumor.

Antibody	Result
Synaptophysin	Negative
Chromogranin A	Negative
NSE	Equivocal positive, weak, regionally variable
Cytokeratin	Equivocal positive, strong, few cells
Calcitonin	Negative
Thyroglobulin	Equivocal positive, weak to moderate, few cells
TTF-1	Positive, weak to strong, diffuse

NSE = neuron specific enolase, TTF-1 = thyroid transcription factor 1

Final diagnosis: Ectopic follicular cell thyroid carcinoma with pulmonary metastasis.

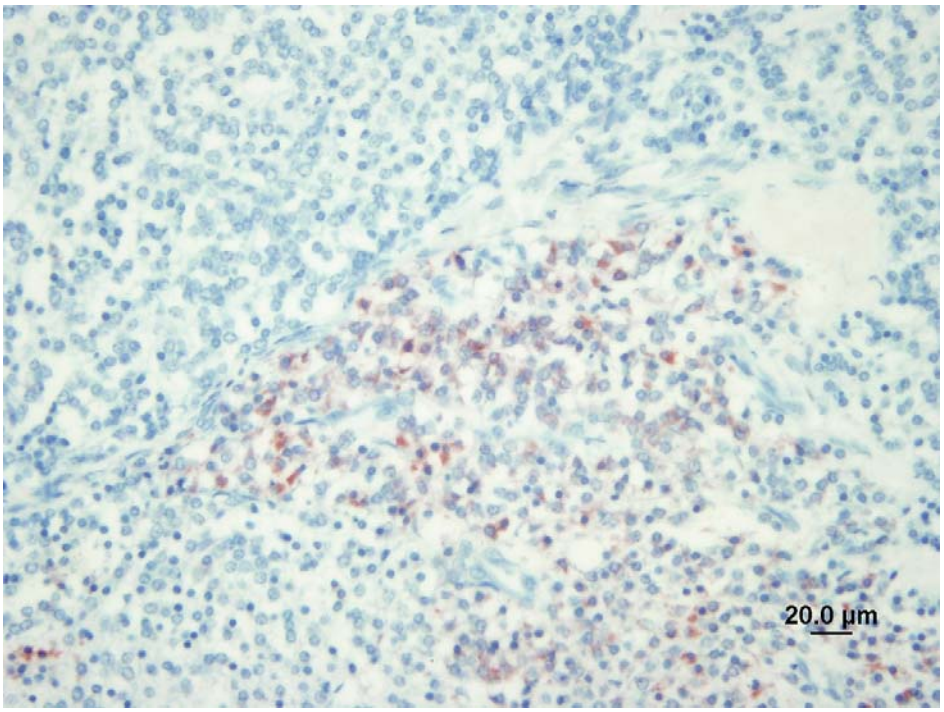

Figure 6. Histologic section of canine heart-base tumor, immunohistochemical stain for thyroglobulin (red cytoplasmic stain), X400 magnification, AEC chromagen.

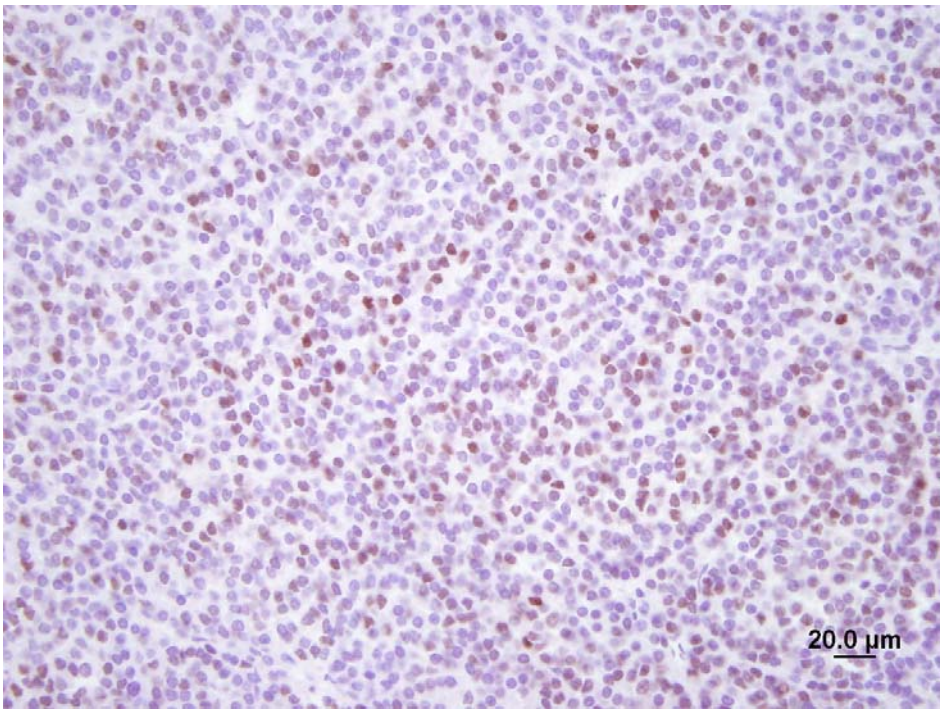

Figure 7. Histologic section of canine heart-base tumor, immunohistochemical stain for TTF-1 (brown nuclear stain), X400 magnification, DAB chromagen.

Discussion: Chemodectoma is the general name for paragangliomas arising from chemoreceptor organs, which include the carotid and aortic bodies.[1] Aortic body tumors arise at the heart base within the pericardium, and with sufficient size cause circulatory disturbances related to compression of the great vessels and atria. Cellular pleomorphism is not sufficient to distinguish adenomas from carcinomas, which are less common. Aortic body carcinomas invade surrounding tissues (aorta, pulmonary artery, pericardium, myocardium) and may infrequently metastasize to the lungs and liver.[2] Like many other neuroendocrine tumors, chemodectomas are typically immunopositive for chromogranin, NSE, and synaptophysin, and don't express cytokeratin.[1] However, loss of immunoreactivity for some of these markers has been reported in malignant tumors of higher grade.[3]

Although the term 'heart-base tumor' has sometimes been used synonymously with 'aortic body tumor', ectopic thyroid tumors are reported to represent 5 – 10% of heart-base tumors in dogs.[2] These tumors are typically composed of follicular cells, but medullary (C-cell) tumors have also been identified.[4] If tumor cells are well-differentiated and forming colloid-filled follicles diagnosis is straightforward, but those exhibiting a solid pattern can be easily mistaken for chemodectoma.[2] Immunohistochemical stains can be helpful in identifying thyroid tissue. Both follicular and medullary thyroid cells can express cytokeratin and TTF-1.[5,6] Follicular thyroid cells also typically express thyroglobulin, while medullary C-cells express calcitonin, chromogranin, synaptophysin, and NSE.[4,6-8] However, there can be considerable variability in the degree to which these markers are detected in any individual tumor, and some anaplastic carcinomas may be immunonegative for all of them. Ultrastructural studies have also been useful in distinguishing between chemodectoma and ectopic thyroid tumors.[9] Ectopic parathyroid tumors are also possible in the mediastinum, but are exceedingly rare in dogs.[10] They would be expected to express typical neuroendocrine markers (chromogranin, NSE, synaptophysin) and PTH.[11]

This case illustrates the difficulty of differentiating heart-base tumors arising from ectopic thyroid versus neuroendocrine tissue, which can have a similar appearance on both cytologic and histologic evaluation. In this case, presence of extracellular eosinophilic material suggestive of colloid on the cytologic specimen made a diagnosis of ectopic thyroid tumor most likely. However, the initial histopathologic diagnosis was neuroendocrine carcinoma, consistent with aortic body tumor/chemodectoma. This discrepancy led us to further characterize the mass using immunohistochemistry.

Diffuse, weak to strong immunoreactivity to TTF-1 was the most convincing evidence that this tumor was actually of thyroid origin. TTF-1 is expressed by lung and thyroid tissues.[6] TTF-1 has been shown to be 93% sensitive for detecting follicular thyroid carcinoma, but is also expressed in some C-cell neoplasms.[6] Thus the combination of TTF-1 and thyroglobulin or calcitonin immunoreactivity is important to evaluate. In this case there was no immunoreactivity to calcitonin, and thyroglobulin immunoreactivity, although present in a minority of cells, supported the final diagnosis of follicular cell thyroid carcinoma. The equivocal positive

immunoreactivity for NSE was confounding. Although NSE is reported to be a sensitive marker for neuroendocrine tissue, concerns about its specificity have been raised before, and the immunoreactivity seen in this case was most likely non-specific.[4,7]

Interestingly, although the cytologic interpretation was swayed by eosinophilic material thought to be colloid, no colloid was observed in the histologic sections from the tumor. Two potential explanations for this discrepancy are that colloid was present in areas of the mass that were aspirated but not sectioned, or else the material seen in the cytologic samples represented some other type of extracellular matrix.

References:

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