**Ectopic Thyroid Carcinoma with Metastases in a Beagle Dog**

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**Abstract.** A 10.25-year-old female beagle had an invasive neoplasm at the base of the heart which metastasized to the lungs, pancreas, and kidney. The neoplasm in these locations was composed of clusters of polyhedral cells surrounded by fine fibrovascular stroma. The differential diagnoses were malignant chemodectoma, ectopic parathyroid carcinoma, and ectopic thyroid carcinoma. Based on ultrastructural features, this tumor was an ectopic thyroid carcinoma.

The differential diagnosis for primary benign and malignant tumors at the base of the heart in dogs includes aortic body tumors (chemodectomas), ectopic parathyroid gland tumors, and ectopic thyroid gland tumors [3]. Malignant chemodectomas are the only heart–base tumors for which there are previous reports of distant metastasis [2–7, 10]. We describe a carcinoma of ectopic thyroid glandular tissue, in a laboratory beagle, which originated at the base of the heart and metastasized widely.

**Case History**

A 10.25–year–old female beagle was one of 120 dogs that received 83 rads of total body $^{60}$Co gamma radiation in utero at day 55 of gestation. The experimental design and dosimetric data for this experiment have been published [1]. The dog had anterior cervical edema with abnormal radiographic densities throughout the lungs and around the base of the heart. Abnormal heart motion and thickening of the pulmonary artery and left ventricular wall were detected by echocardiography. Electrocardiographic conduction disturbances also were present. The dog was killed and a thorough postmortem examination was done.

**Materials and Methods**

Gross lesions and representative samples of all major body organs were collected and fixed in 10% neutral buffered formalin, embedded in paraffin, sectioned at 6 μm, and stained with hematoxylin and eosin (HE). Sections of neoplasms also were stained with periodic acid–Schiff (PAS). Representative samples of the masses at the base of the heart and in the left kidney were fixed in 2.5% glutaraldehyde, postfixed in osmium tetroxide, and embedded in epoxy
resins. Sections from the heart and kidney tumor masses were cut at 1 μm and stained with Azure II–methylene blue–basic fuchsin. Selected specimens were cut in ultrathin sections, stained with uranyl acetate and lead citrate, and examined on an electron microscope.

**Results**

Necropsy showed a white, friable, 8–cm diameter, multinodular mass at the base of the heart. It had invaded the right atrium, right auricle, pulmonary artery, interatrial septum, and dorsal interventricular septum. It also had extended into the pericardial sac and spread over the epicardial and pericardial surfaces. Many white nodules up to 2 cm in diameter were scattered throughout the pancreas and both lungs. The cortex of the left kidney contained a discrete 6 × 4–cm mass that bulged from its cut surface. Both lobes of the thyroid gland and all parathyroid glands were normal sized.

The histology of all masses associated with the heart, lungs, pancreas, and left kidney was similar. The cells in these masses were polyhedral with lightly eosinophilic, finely granular, and occasionally vacuolated cytoplasm. Widely scattered cells contained PAS–positive intracytoplasmic droplets or globules. Nuclei varied in size and shape, but most were round to oval and usually centrally located. Chromatin was finely granular and nuclei occasionally contained a single large round amphiphilic nucleolus. There were three to six mitotic figures per high-power field (fig. 1). The cells were arranged in sheets or nests and lobules that were surrounded by fine fibrovascular connective tissue. In the right atrium, pancreas, and kidney, they invaded surrounding connective tissue and blood vessels (fig. 2). The masses in the lungs were well demarcated from surrounding tissue. The right lobe of the thyroid gland had a small noncircumscribed nodule of hyperplastic follicular cells. This nodule was composed of orderly clusters of follicular cells and a few well-formed follicles. The periphery of the nodule either blended with surrounding normal thyroid tissue or compressed adjoining follicles. The other thyroid lobe and all parathyroid glands were free of pathologic changes. Other findings were generalized lymphoid hyperplasia, a chromophobe adenoma of the pars intermedia of the pituitary gland, bilateral adrenal cortical hyperplasia, and a granulosa cell tumor with a Sertoli cell pattern in the left ovary.

Ultrastructurally, the neoplastic cells in the myocardial mass had irregular, interdigitating cytoplasmic borders that often were associated on at least one surface with a basement membrane (fig. 3). These cells often formed intracellular or intercellular lumina with villous projections. The cytoplasm was dense. It contained occasional lipid droplets, many free ribosomes and polyribosome complexes, and moderate numbers of large lysosomes and mitochondria. The latter frequently were swollen. Flattened parallel cisternae of rough endoplasmic reticulum usually were present; occasionally, however, the rough endoplasmic reticulum formed concentric layered whorls that sometimes surrounded groups of mitochondria. Occasionally, tumor cells of the heart mass contained tubular structures composed of a highly electron-dense
Fig. 1: Mass from base of heart. Sheet of pleomorphic polyhedral cells with many mitotic figures. HE.

Fig. 2: Neoplastic invasion of the myocardium of the right atrium. HE.
Fig. 3: Myocardial mass of interdigitating cells with associated basement membranes and intracellular lumina (top right). Lead citrate and uranyl acetate.

...core and separated from the limiting membrane by a clear zone of variable width (fig. 4).

The renal mass was composed of similar cells, although associated basement membranes and luminal structures were less frequent (fig. 5). The rough endoplasmic reticulum in this metastatic portion of the tumor was extensive, quite irregular, usually dilated, and closely associated with many mitochondria, which occasionally had tubular cristae. Tubulated structures, which clearly were associated with the rough endoplasmic reticulum, were found in tumor cells (fig. 6). These structures occurred as single or multiple paired electron-dense lines within the dilated endoplasmic reticulum cisternae when sectioned obliquely or tangentially, and as groups of uniform round tubules in cross section.

**Discussion**

Ultrastructural characteristics may be the only way to accurately differentiate some aortic body tumors, ectopic parathyroid gland tumors, and ectopic thyroid gland tumors originating at the base of the heart in dogs. Malignant aortic body tumors, which are less common than benign tumors of this tissue in dogs [2], have been
Fig. 4: Tubular structures composed of electron-dense core with limiting membranes. Lead citrate and uranyl acetate.

Fig. 5: Renal mass; neoplastic cells contain many mitochondria. In some cells the endoplasmic reticulum is prominently dilated. Lead citrate and uranyl acetate.

Fig. 6: Bundles of tubulated structures cut in various planes of section; renal mass. Lead citrate and uranyl acetate.
reported to invade locally the atria, the walls of great vessels, and the pericardium, epicardium, and myocardium [2, 4, 7, 10]. Metastases to regional lymph nodes, lungs, spleen, liver, pancreas, kidney, and bone have been reported [2–7, 10]. Neoplastic cells of aortic body origin are characterized ultrastructurally by the presence of electron-dense, membrane-bound cytoplasmic granules [3, 6]. A malignant ectopic (mediastinal) parathyroid tumor, which must be considered in the differential diagnoses of tumors in this region, has been described in the dog [8]; this tumor infiltrated local blood vessels and the heart, but did not metastasize to distant sites. Tumor cells of parathyroid gland origin are characterized by a scarcity of cytoplasmic organelles and the absence of membrane-bound granules [3, 8]. Thyroid adenomas and carcinomas of the thyroid gland and of ectopic thyroid tissue at the base of the heart have ultrastructural characteristics including well-developed cytoplasmic organelles, variable numbers of large intracytoplasmic vacuoles, absence of membrane-bound dense granules, and distinctive tubular or rod-like structures in the cytoplasm [3, 11].

The ultrastructural features of the tumor in this beagle are therefore like those described for tumors of thyroid gland origin. The right lobe of the thyroid gland contained a small hyperplastic nodule; however, no malignant neoplasm was found in either lobe of the thyroid gland. Consequently, a diagnosis of ectopic thyroid carcinoma was made. It has been estimated that approximately 50% of all dogs have ectopic thyroid tissue in the mediastinum and around the base of the heart [9]. Nonetheless, ectopic thyroid carcinomas are uncommon canine neoplasms. This one is unique because of its invasive growth and widespread metastasis.

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References

1 Angleton, G.M.; LoPresti, C.A.: A summary of the dosimetrics for exposures to 60Co of the beagles entered into the CRHL long-term study. Health Phys 33:100–103, 1977


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