Pathology in Practice

In collaboration with the American College of Veterinary Pathologists

History

A 3-year-old 400-g sexually intact male bearded dragon (Pogona vitticeps) was presented to the University of Tennessee College of Veterinary Medicine exotic medicine and surgery service for a chronic history of progressive anorexia and lethargy.

Clinical and Gross Findings

On physical examination, the bearded dragon had a palpable cranial coelomic mass. Abnormal clinicopathologic values included hyperglycemia (1,348 mg/dL; reference range, 1210 to 255 mg/dL) and mild anemia (PCV, 21%; reference value, 27%). Ultrasonography highlighted a gastric mass with multiple liver masses. Because of the poor prognosis, euthanasia was performed via intracardiac administration of sodium pentobarbital. The bearded dragon was submitted for necropsy.

Histopathologic Findings

Portions of the stomach, liver, kidneys, coelomic fat bodies, spleen, tail muscles, pancreas, and heart were fixed in neutral-buffered 10% formalin and processed routinely, and sections were stained with H&E stain for histologic examination. Expanding and effacing the gastric submucosa, compressing the adjacent mucosa, and extending into the muscularis externa was an unencapsulated, well-demarcated neoplasm composed of trabeculae, cords, and packets of

Bianca R. Pfisterer, DVM*; Nathan K. Hoggard, DVM; Mee-Ja M. Sula, DVM

Department of Biomedical and Diagnostic Sciences, College of Veterinary Medicine, University of Tennessee, Knoxville, TN

*Corresponding author: Dr. Pfisterer (Bianca-Pfisterer@idexx.com)

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neoplastic polygonal cells within a moderate fibrovascular stroma (Figure 2). Neoplastic cells had indistinct cell borders, scant to moderate amounts of pale eosinophilic cytoplasm, a round to oval nucleus with coarse chromatin, and indistinct nucleoli. Anisocytosis and anisokaryosis were mild, with rare cells and nuclei up to 6 times the size of adjacent neoplastic cells and nuclei. There were 30 mitotic figures/10 hpf (at 400X magnification). A few lymphatics within the submucosa were filled with islands of neoplastic cells.

Immunohistochemical staining with antisomatostatin, anti-insulin, and antigastrin antibodies was performed on the gastric neoplasm at Purdue University with standard positive and negative canine controls. Approximately 30% of the neoplastic cells had moderate to strong granular cytoplasmic immunoreactivity to somatostatin (Figure 2). Neoplastic cells were immunonegative for gastrin and insulin. Immunohistochemical staining with antiglucagon antibodies was attempted, but inadequate labeling of positive controls resulted in an unsuccessful assay. Immunohistochemical staining of metastases was not performed.

Hepatocytes were diffusely expanded by clear, round cytoplasmic lipid vacuoles. Unencapsulated, well-demarcated masses composed of neoplastic cells similar to those described for the gastric neoplasm multifocally and randomly expanded and effaced the hepatic parenchyma. The kidneys, fat bodies (Figure 2), spleen, hypaxial tail muscles, pancreas, omentum, and myocardium had similar neoplasms.

**Morphologic Diagnosis and Case Summary**

Morphologic diagnosis and case summary: gastric neuroendocrine carcinoma with hepatic, omental, splenic, renal, skeletal, muscular, pancreatic, myocardial, and coelomic fat body metastases.

**Comments**

The clinicopathologic finding of severe hyperglycemia paired with the clinical signs and gastric ultrasonographic findings were typical for gastric neuroendocrine carcinoma in bearded dragons, and the diagnosis was confirmed with gross necropsy and histopathologic findings. Reported neoplasms in bearded dragons include but are not limited to gastric neuroendocrine carcinomas, peripheral nerve sheath tumors, lymphoid and myeloid leukemias, squamous cell carcinomas, periocular myxosarcomas, and iridophoromas, with neuroendocrine carcinomas being the most common primary gastric neoplasm. The
liver is the most frequent site of metastasis, with other less frequent sites of metastasis consisting of the kidneys, pancreas, intestines, heart, and reproductive tract. To our knowledge, metastasis of a gastric neuroendocrine carcinoma to the fat bodies and skeletal muscle in a bearded dragon has not been reported previously.

The diagnosis of a neuroendocrine carcinoma can be confirmed with immunohistochemical staining for chromogranin A, synaptophysin, and neuron-specific enolase. Use of more specific antibodies for somatostatin, gastrin, glucagon, insulin, and serotonin, which are hormones these neoplasms can secrete, is often beneficial to determine more definitively the cell of origin. Gastric neuroendocrine carcinomas in bearded dragons are reported to have primarily cytoplasmic immunoreactivity for somatostatin and, much less frequently, mixed immunoreactivity for somatostatin, gastrin, or glucagon. Neoplastic cells in this case had moderate cytoplasmic immunoreactivity for somatostatin only, which is suggestive of a somatostatinoma; however, blood somatostatin concentrations were not evaluated for confirmation. Somatostatin causes a decreased release of the anterior pituitary hormones, growth hormone, thyroid stimulating hormone, adenyl cyclase, and prolactin.

Somatostatin-producing tumors in humans cause a syndrome known as somatostatinoma syndrome. In these patients, concurrent hyperglycemia, diabetes mellitus, anemia, and gallstones develop. Local gastrointestinal effects include decreases in gastric emptying; smooth muscle contractions; and insulin, glucagon, gastrin, secretin, and pancreatic zymogen granule release. The inhibition of insulin and glucagon release is the proposed mechanism for the development of hyperglycemia in humans through an inability to decrease circulating blood glucose concentrations and decreased hepatic gluconeogenesis, respectively. The cause of anemia in somatostatinoma syndrome remains unclear, but it is speculated to be paraneoplastic anemia or anemia of chronic inflammation. Both anemia and hyperglycemia have been reported in bearded dragons with somatostatin-immunoreactive gastric neuroendocrine carcinomas, as in this case, and the condition has been suggested to be similar to somatostatinoma syndrome in humans. Although cholelithiasis is reported in somatostatinoma syndrome in humans, it was not present in this case or in the previously reported bearded dragons with neuroendocrine carcinomas.

References