History

A 1.5-year-old male bearded dragon (Pogona vitticeps) was presented to the Atlantic Veterinary College for evaluation following 4 weeks of progressively declining health. During the month preceding presentation, the bearded dragon reportedly became lethargic and anorexic and appeared dull in color. Prior to the onset of clinical signs, the patient was provided a well-balanced diet, and appropriate husbandry was maintained based on species requirements.

Clinical and Gross Findings

On physical examination, the bearded dragon was lethargic with evidence of dehydration and weight loss (body condition score, 2/9), characterized by sunken eyes, prominent pelvic bones, and thin limbs. A CBC revealed marked heterophilic leukocytosis (leukocytes, 75 × 10^9 cells/L; reference interval, 1.45 × 10^9 to 19.0 × 10^9 cells/L), with a mild left shift (heterophils, 42 × 10^9 cells/L; reference interval, 0.24 × 10^9 to 7.77 × 10^9 cells/L); and band heterophils, 6 × 10^9 cells/L), marked toxic changes, and marked monocytosis (monocytes, 18.7 × 10^9 cells/L; reference interval, 0.03 × 10^9 to 1.39 × 10^9 cells/L). Plasma biochemical analyses revealed marked hyperglycemia (82.4 mmol/L; reference interval, 16 to 18.5 mmol/L) and marked hyperuricemia (2,386 µmol/L; reference interval, 127 to 544 µmol/L). Orthogonal 2-view full-body radiography revealed radiographically normal bone opacity and no obvious pathology.

Given the severity of changes on bloodwork and the patient’s declining clinical condition, euthanasia was discussed with the owner. Antimicrobial treatment was also discussed but declined in favor of supportive care. One week later, the bearded dragon was again presented to the hospital due to a lack of improvement. Repeat venipuncture was performed; blood glucose and uric acid concentrations were reassessed and revealed persistent marked hyperglycemia (74.6 mmol/L) and a worsened hyperuricemia (> 7,440 µmol/L). A blood sample was also submitted for aerobic culture and susceptibility testing because of suspected sepsis. Based on the animal’s declining health and clinical pathology findings, the owner elected to euthanize the bearded dragon and consented to postmortem examination. Blood culture results returned following euthanasia and revealed growth of Pseudomonas aeruginosa.

On gross postmortem examination, a single 1-cm-diameter nodular white-yellow mass was present in the gastric wall (Figure 1). Numerous 0.3- to 2.0-cm-diameter nodular yellow masses were scattered throughout the liver. A small amount of turbid fluid and yellow friable material was present in the coelomic cavity and pericardial sac. The lungs contained multiple irregular yellow nodular foci with fibrin adhered to the pleural surface. Additional

Jenna M. Thebeau, DVM; Shannon A. Martinson, DVM, MVSc; Noel P. Clancey, DVM, MVSc; Oriana D. Raab, DVM, MVSc

1Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada
2Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK, Canada
3Department of Companion Animals, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada
4Department of Pathology and Microbiology, Atlantic Veterinary College, University of Prince Edward Island, Charlottetown, PE, Canada

*Corresponding author: Dr. Raab (oraab@upei.ca)

https://doi.org/10.2460/javma.21.02.0077

Figure 1—Postmortem photograph of the stomach and liver from a 1.5-year-old bearded dragon (Pogona vitticeps) with hyperglycemia and a 4-week history of progressively declining health. A 1-cm white-yellow nodular mass is present in the gastric wall, and the liver contains multiple 0.3- to 2.0-cm white-yellow nodular masses.
testing included aspirates and impression smears of liver masses, histopathology, and aerobic bacterial culture of pericardial fluid and liver tissue.

Formulate differential diagnoses, then continue reading.

**Cytologic and Histopathologic Findings**

Hepatic aspirates and impression smears contained moderate numbers of tissue cells, mild blood contamination, and numerous free nuclei on a nonstaining background. Tissue cells were often present individually or in loosely to densely packed, variably sized clusters and rarely in small cohesive sheets (Figure 2). Rare acinar-like arrangements were also present. Most cells had neuroendocrine morphologies. Rare well-differentiated hepatocytes, bland spindeloid mesenchymal cells, and macrophages containing phagocytized debris were also present. Cells with neuroendocrine features were approximately 10 to 20 µm in greatest diameter, often had ill-defined margins, yet were polygonal, rounded to spindeloid where better defined. Cells had a high nuclear-to-cytoplasmic ratio and small volumes of pale blue-gray foamy cytoplasm occasionally containing 1 to 5 small round clear vacuoles. Nuclei were round to ovoid with coarsely stippled to clumped chromatin and occasionally contained small round nucleoli. Anisocytosis, anisokaryosis, and variation in the nuclear-to-cytoplasmic ratio were moderate. Nuclear molding was frequently observed and occasional binucleated cells were present. Interpretation was malignant neoplasia, likely of endocrine or neuroendocrine origin.

On histopathology, a highly cellular, well-defined, unencapsulated nodular mass was present in the stomach invading the submucosa and the ulcerated mucosa (Figure 3). The mass was composed of solid lobules of neoplastic cells supported by a fine collagenous stroma, with occasional lobules containing small central foci of necrosis. Neoplastic cells were polygonal with ill-defined cell margins, small amounts of flocculent eosinophilic cytoplasm, and a large round to ovoid nucleus. The cells exhibited moderate anisocytosis and anisokaryosis, occasional marked karyomegaly, and a mitotic rate of 66 mitoses/10 hpfs (400X). The liver masses were similar in composition. These findings were compatible with a gastric neuroendocrine (NE) carcinoma and hepatic metastasis. Immunohistochemical testing for somatostatin was performed at the Veterinary Diagnostic Laboratory, University of Minnesota. Small numbers of tumor cells showed positive cytoplasmic staining for somatostatin. Other important histological findings included multifocal granulomatous and heterophilic pleuropneumonia, hepatitis, nephritis, encephalitis, as well as fibrinous coelomitis and pericarditis. Gram-negative bacilli were identified within these lesions confirming septicemia. Lipid vacuoles were present within hepatocytes and renal tubular epithelial cells, warranting a diagnosis of hepatic and renal tubular lipidosis. Urate stasis was evident in the kidneys, suggesting dehydration.

Pericardial sac and hepatic aerobic bacterial culture revealed moderate growth of *Pseudomonas aeruginosa* and light growth of *Pseudomonas aeruginosa* and *Citrobacter freundii*, respectively.

**Morphologic Diagnosis and Case Summary**

Gastric neuroendocrine carcinoma with hepatic metastasis and secondary bacterial sepsis in a bearded dragon.
A syndrome of hyperglycemia associated with gastric NE carcinomas in young bearded dragons has emerged over the past decade. In all reported cases, gross and histologic examination revealed primary NE carcinoma in the gastric submucosa with metastasis primarily to the liver similar to this case. Several bearded dragons also exhibited metastasis to other organs such as kidney, intestine, pancreas, heart, spleen, lung, and oviduct.

Variable positive expression of somatostatin in NE carcinomas in bearded dragons has been previously reported and was present in this case in rare scattered tumor cells. In humans, somatostatin has been reported to suppress insulin, glucagon, pancreatic peptides, gastrin, gastric acid secretion, gastric motility, intestinal absorption, and gall bladder contraction. Human somatostatinomas create a syndrome characterized by gastrointestinal signs, weight loss, diabetes mellitus, cholelithiasis, hypochlorhydria, anemia, and exocrine pancreatic insufficiency.

Bearded dragons with somatostatin-expressing NE carcinomas (often referred to as somatostatinomas) have typically been young (1.5 to 3 years), with clinical signs of progressive inappetence, weight loss, and lethargy similar to the patient in this case. Gastrointestinal disturbances, such as vomiting, have also been reported. Clinicopathologic abnormalities have included anemia, hyperglycemia,
heterophilic leukocytosis with a left shift, monocytosis, and lymphopenia. The clinical signs and clinicopathologic abnormalities highlighted in the present report were strikingly similar to previous reports in bearded dragons. Hemorrhage from ulcerative gastric tumors, hematic loss from septicemia, or anemia of chronic disease provide possible explanations for anemia in affected patients. Although the hematocrit for this patient was within reference limits, it was possible that anemia was masked by concurrent dehydration. Bloodwork abnormalities associated with these tumors in bearded dragons have consistently shown anemia, hyperglycemia, or both. The marked hyperglycemia observed in this patient was comparable to that previously reported including glucose concentrations of 50, 54, and 90 mmol/L. Marked hyperglycemia in young bearded dragons has few causes. Aside from somatostatin-secreting neoplasms, hyperglycemia in bearded dragons can be due to diabetes mellitus and pancreatitis with stress-associated hyperglycemia, seasonal variations, postprandial hyperglycemia, and anorexia as possible contributing physiologic sources. Although diabetes mellitus or persistent hyperglycemia is rarely described in reptiles, pancreatic islet damage due to pancreatitis, trauma, or autoimmune disease leading to decreased insulin production can result in hyperglycemia similar to other species. However, in this case, no pancreatic abnormalities were observed on histology.

Leukocytoses in documented cases of bearded dragons with somatostatin-expressing NE carcinomas likely reflect inflammation associated with the neoplasms itself or sepsis. In the patient of the present report, the aggressive nature of the tumor resulted in gastric mucosal ulceration, providing an entry point for opportunistic bacteria such as P aeruginosa and C freundii, leading to septicemia. The neoplastic disease process, septicemia, and widespread organ bacterial infiltrates supported the substantial inflammatory response evident on bloodwork. Hyperuricemia was also noted in this case, likely reflecting a combination of dehydration and renal damage associated with bacterial nephritis.

Marked hyperglycemia may provide a more sensitive screening tool for somatostatin-secreting neuroendocrine tumors in bearded dragons. Other noninvasive antemortem diagnostic techniques for this disease are limited. Radiography, ultrasonography, CT, and MRI can identify discrete masses. However, limited availability and proficiency of clinicians in interpreting obtained images of this species restrict the successful use of these diagnostic modalities. Recommendations include obtaining images of clinically normal bearded dragons to use for comparison prior to evaluating the diseased patient. Cytology may be a useful tool for diagnosing tumors in reptiles and recently, the cytologic description of this tumor has been well described. The present case provided an additional resource for identifying this tumor cytologically. Ultrasound-guided fine-needle aspiration could lead to a more specific antemortem diagnosis, as NE cells exfoliate readily. Of note, antemortem fine-needle aspirate samples should be obtained from hepatic metastases as opposed to gastric masses due to the risk of perforation. Currently, these tumors are typically diagnosed on postmortem examination based on gross and histologic appearance combined with immunohistochemistry for somatostatin.

This case report highlights the need for earlier diagnosis and additional research into the variables involved in the emergence of these tumors in young bearded dragons. Clinicians should consider this neoplasm when presented with a young bearded dragon with vague clinical signs and persistent hyperglycemia.

References