Pathology in Practice

An 8-month-old male bearded dragon (Pogona vitticeps) was evaluated at the University of Illinois Veterinary Teaching Hospital because of a mass on the upper eyelid of the right eye. The mass was first noticed by the owner 3 days earlier. The lizard had been acquired 7 months prior to the evaluation from a private breeder and was housed in a 20-gallon tank on sand substrate. The lizard's diet consisted of a daily ration of vegetables and crickets (gut-loaded with calcium supplement) and occasional waxworms. Full-spectrum UV lighting and supplemental heat were used appropriately in the lizard's enclosure; the daytime temperature reached 40°C (104°F), and the evening temperature was maintained at 36.7°C (98°F). The bearded dragon did not have regular contact with other animals; its last contact with other bearded dragons was 3 months earlier.

Clinical Findings

A physical examination revealed that the bearded dragon was bright, alert, and responsive. It had a body weight of 88 g (0.19 lb) and was in good body condition. There was an approximately 4-mm-diameter exophytic, broad-based mass arising from the dermal aspect of the upper medial palpebra of the right eye (Figure 1). No corneal, conjunctival, or anterior segment abnormalities were evident in either eye. Findings of coelomic palpation were considered normal, with minimal palpable fat pad. All limbs appeared to be normal. No oral lesions were detected. A fine-needle aspirate sample of the mass was obtained for cytologic examination; findings were nondiagnostic and consistent with peripheral blood. Resection and histologic evaluation of the mass were performed.
Histopathologic Findings

Histologic examination of sections of the excised eyelid mass revealed a poorly demarcated, moderately cellular neoplastic mass composed of small, occasionally interconnecting nests of squamous epithelial cells supported by a dense fibrovascular stroma (Figure 2). The cells had a moderate to abundant amount of glassy and fibrillar eosinophilic cytoplasm with variably distinct cell borders. Intercellular bridging was rare. Nuclei were round to ovoid and faintly basophilic, with coarsely clumped or vesicular chromatin and up to 3 small but prominent nucleoli. There was marked anisocytosis and anisokaryosis, with a low mitotic index (1 mitotic figure/10 hpf [400X]). There was evidence of asynchronous differentiation among the neoplastic cells; some nests of cells contained centrally located accumulations of eosinophilic, compacted, lamellated, and occasionally concentrically oriented keratin (keratin pearls). Neoplastic cells extended to the surgical margins in the sections examined. The stroma contained moderate numbers of granulocytes with fewer monocytes. Immunohistochemical analysis with antibodies against cytokeratins AE1 and AE3 yielded moderate to strong cytoplasmic labeling of the neoplastic cells in sections of the mass (Figure 3).

Morphologic Diagnosis

Squamous cell carcinoma (SCC) of the skin of the upper right eyelid.

Comments

Neoplasia is increasingly identified as a disease process in reptiles. Results of retrospective studies1–3 in chelonians, snakes, lizards, and crocodilians have indicated that skin tumors are relatively common and include such tumors as SCCs, melanomas, fibrosarcomas, cutaneous papillomas, fibropapillomas, lipomas, spindle cell sarcomas, and chromatophormas. In 1 report,1 skin tumors represented approximately 22% of 98 masses removed from reptiles during biopsy or necropsy and submitted for evaluation. Cutaneous SCC, specifically, has been identified in various species of snakes, lizards, and turtles1–10 and is typically well differentiated, locally invasive, and rarely metastatic.5 One study2 determined that the overall tumor prevalence in lizards was 8.5%; in that study, 1,901 individuals were evaluated and 9 of 162 (5.6%) neoplasms were identified as SCCs. No SCC was diagnosed in bearded dragons from that study.2 The only previously documented report4 of SCC in a bearded dragon was that of a tumor associated with a palpebral lesion in an adult. In contrast to bearded dragons, SCC is a common skin tumor in cats and dogs, accounting for approximately 15% and 5% of cutaneous tumors in those species, respectively.11 In cats and dogs, the tumors typically develop in areas of unpigmented or lightly pigmented skin as well as sparsely haired areas.11 Potential associations identified with SCC formation in small animals include solar exposure (actinic SCC) and papillomavirus.11 Current treatments for SCCs include resection and cryosurgery, although radiation therapy, photodynamic therapy, chemotherapy (single agent, adjunctive, and intraleisional), and administration of...
synthetic vitamin A retinoids or piroxicam have also been reported as potential treatment options.\textsuperscript{11} To the authors’ knowledge, the present report is the first in which positive results of immunohistochemical labeling of sections of an SCC with a pancytokeratin marker in a reptile are described. Although labeling of the skin of lizards with markers for cytokeratins has yielded positive results previously,\textsuperscript{12} there was no uptake of those labels by normal epithelial cells and neoplastic cells in SCCs in loggerhead sea turtles.\textsuperscript{8} Follow-up testing revealed that the markers used on the sections of tumor removed from the bearded dragon of the present report also labeled normal epithelial cells from the skin of a bearded dragon and a Blanding’s turtle. Possible reasons for differences among the results include variations in epitope recognition or binding affinity among the antibodies used, technical difficulties that prevent successful labeling, or differential expression of α-keratin, a high–molecular-weight keratin (40 to 70 kDa) that is the target of the anti-pancytokeratin antibodies used in the case described in the present report and in a previous study\textsuperscript{9} of epithelial cells collected from loggerhead and Blanding’s turtles. Reptile epithelial cells switch from synthesizing α-keratin to smaller β-keratins (10 to 30 kDa) as the cells migrate and mature, and this is known to be a seasonal phenomenon.\textsuperscript{13}

In the case described in the present report, debulking surgery and cryosurgery were performed to treat the lesion. The mass was excised at the base parallel with the eyelid, removing all but approximately 1 mm of raised tissue at the base of the mass. Two freeze and thaw cycles of cryotherapy with liquid nitrogen were applied directly to the remaining mass followed by chemical cautery by use of a silver nitrate stick. Cryosurgery uses cold temperature to induce cellular death.\textsuperscript{4} Direct cellular death occurs secondary to ice crystal disruption of cellular membranes, electrolyte changes, alteration of cellular proteins, and thermal shock. Cryosurgery also causes cellular death via vascular collapse, in which small blood vessels and capillaries are irreversibly damaged, inducing hypoxia and infarction of frozen tissues. In general, cryosurgery is recommended for small (< 2.5 cm) and benign or locally invasive tumors only. The eyelid is a common site for application of this treatment technique in other species; frequently, the zone of freezing extends through the full thickness of the eyelid, which results in good cosmetic and functional outcomes.\textsuperscript{15} Cryotherapy was chosen for treatment of the bearded dragon of the present report because complete simple surgical excision would have impaired eyelid function. Furthermore, aggressive excision prior to cryotherapy was not pursued in this small patient because of the concern for postoperative thinning or necrosis of the eyelid. A follow-up report on the bearded dragon obtained approximately 8 weeks after surgery indicated that the patient was doing well and the eyelid had healed well.

At this time, the cause of SCC in reptiles, and specifically bearded dragons, is undetermined. Solar radiation exposure, higher altitude, and a white or piebald coat have been identified as risk factors for SCC in mammalian species.\textsuperscript{18} In reptiles, it is possible that the adnexa surrounding the eye is more susceptible to UV damage because of its prominent location and meager amount of protective scales; however, given the young age of the bearded dragon of the present report, chronic exposure to UV radiation was not likely an important factor contributing to the formation of the tumor. An association of SCC development with viral infection in this patient may be a reasonable consideration. Papillomavirus has been isolated from 30 of 63 SCC in situ skin lesions in cats, and papillomavirus lesions in kittens as young as 6 to 7 months old have been reported.\textsuperscript{17} In reptiles, herpesvirus, poxvirus, and papovavirus infections have been associated with neoplastic conditions.\textsuperscript{6} Tissues from the patient of the present report were not submitted for viral examination. Further investigation into a viral cause of or contribution to neoplasia in reptiles, specifically SCC in bearded dragons, is warranted.

a. Biogenex, Fremont, Calif.
b. Cry-AC unit, BrynMawr Cryogenics, Ellington, Conn.

References