

Case Report

Successful Treatment of Cutaneous Squamous Cell Carcinoma in a Captive Green Iguana (*Iguana Iguana*)

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A B S T R A C T

Reptiles are popular exotic pets and green iguanas (*Iguana iguana*) are amongst the top ten most popular reptiles. Here we describe a captive 8-year-old female green iguana that was referred for treatment of a non-healing, discharging lesion on the side of the body. The lesion was surgically excised and histopathological analysis revealed an epidermal proliferation of neoplastic keratinocytes, with focal infiltration through the basement membrane, into the underlying superficial dermis. Marked dysplastic changes, characterized by multifocal dyskeratosis and keratin pearl formation were also noted. A diagnosis of cutaneous squamous cell carcinoma (SCC) was made. Two years later, the iguana has shown no signs of recurrence. This is the first report of successful treatment of cutaneous SCC in a green iguana and contributes to the limited knowledge of cutaneous neoplasms in green iguanas.

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Introduction

Reptiles are one of the most popular exotic pets,¹ with the largest reptile consumer markets present in the United States of America and Europe, where a combined total of over 9 million reptiles are kept as pets.² Green iguanas (*Iguana iguana*) are one of the top ten most popular reptiles,² and are commonly found in captivity as pets or zoo and/or wildlife park exhibits due to their calm disposition and bright colors. The green iguana is a large, diurnal, arboreal, mostly herbivorous lizard that ranges over a large geographic area, with its native range extending from southern Mexico to the Caribbean to central Brazil, Bolivia, and Paraguay.³

Amongst the reptile species, lizards have a similar incidence of neoplastic disease as snakes, turtles, and tortoises, although one retrospective study found that iguanas and chameleons had a lesser prevalence than monitors, skinks, agamids, and geckos (3.4%–3.9% vs. 7.7%–9.9%, respectively).^{4–5} The most commonly reported single neoplasia of lizards is lymphoma.^{4,6} Squamous cell carcinoma (SCC), typically occurring in the skin or oral cavity, is a malignant tumor that has been reported in several lizard species.^{4–6} Similar to other species, SCC in lizards is commonly slow growing and shows local invasion but rarely metastasizes, with surgical excision frequently being curative if excision is complete.⁶ There has been a report of a cutaneous

SCC in a green iguana as part of a retrospective review of neoplasms of captive lizards in the United Kingdom over a 10-year period,⁷ however, there have been no case reports detailing the presentation of the lesion, its histopathological features, treatment and outcome with long-term follow up. The case detailed here is the first detailed case report of SCC in a green iguana, which presented as a non-healing wound and was successfully treated with surgical excision.

Case History

An 8-year-old female green iguana living at the Lory Park Zoo and Owl Sanctuary in Midrand, South Africa had a lesion on her left flank for approximately 2 years. In the space of a few weeks the lesion had started to increase in size and was noticeably protruding with a serous discharge and no indication of healing. The iguana was restrained and a regional anesthetic block was performed using 2% lignocaine locally infiltrated around the lesion (1 mg/kg, Pfizer South Africa, Sandton, South Africa). Meloxicam was administered intramuscularly (0.2 mg/kg, Petcam, Cipla Medpro Ltd, Bellville, South Africa) and the ~0.5 cm diameter lesion was then surgically excised with a 0.5 cm margin. The lesion was placed into 10% buffered formalin and the wound was closed with vertical mattress sutures using synthetic absorbable monofilament surgical suture material (Monosyn 3/0, Braun Surgical S.A. Northriding, South Africa).

The lesion was sent for histopathological analysis. H&E-stained sections of the tissue sample revealed an epidermal proliferation of neoplastic keratinocytes, with multifocal infiltration through the basement membrane, into the underlying superficial dermis (Fig 1). Also noted

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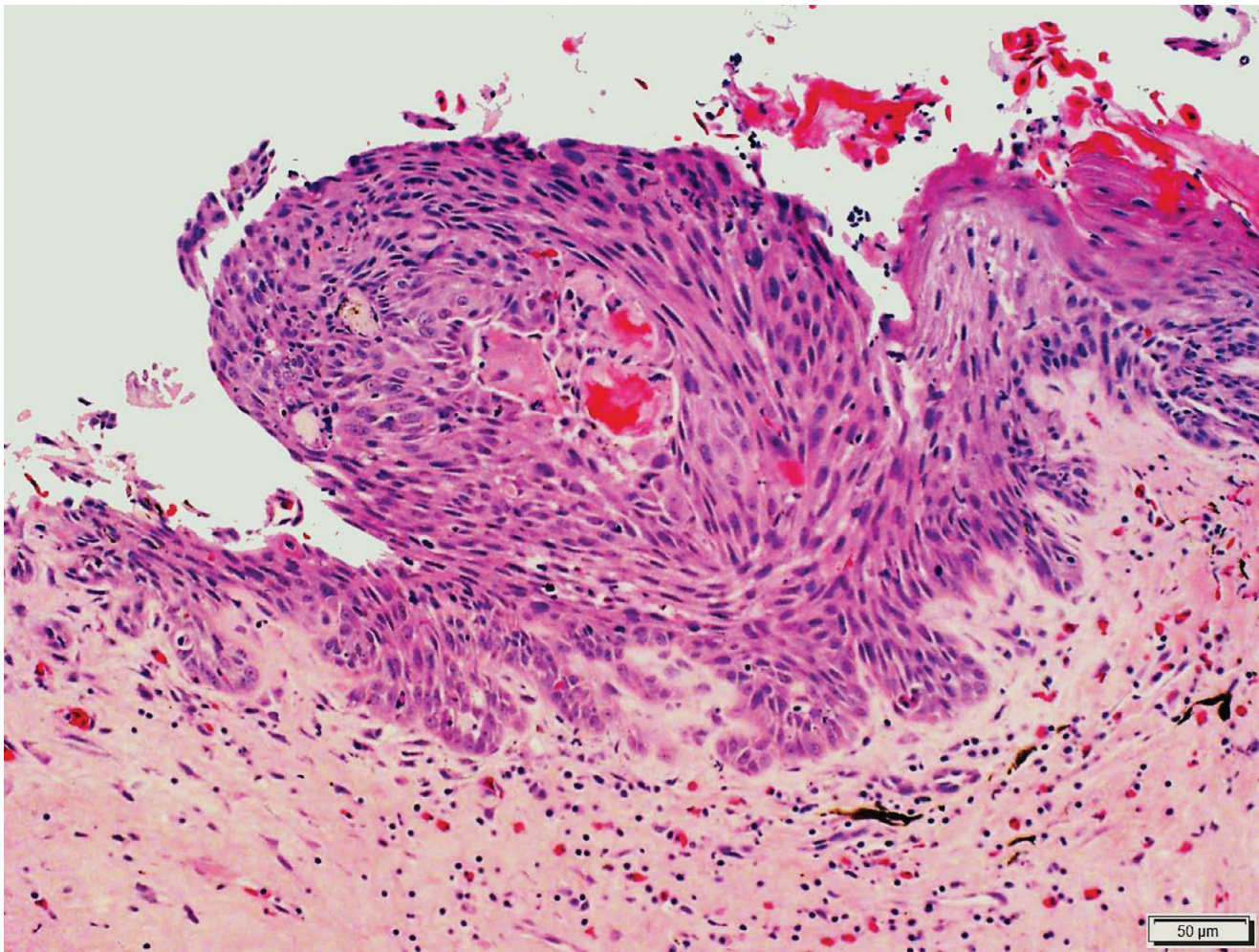


Fig 1. *Iguana iguana*, cutaneous squamous cell carcinoma. Epidermal proliferation of neoplastic keratinocytes, with surface erosion and multifocal infiltration through the basement membrane, into the underlying superficial dermis. Haemorrhage is also present. H&E. Bar = 50 μ m.

were marked dysplastic changes, characterized by multifocal dyskeratosis and the formation of small keratin pearls (Fig 2). The neoplastic cells were pleomorphic, varying from predominantly spindlyoid to epithelioid, with predominantly round to oval nuclei, finely stippled chromatin and one to two prominent central nucleoli. The cytoplasm of the neoplastic cells was moderate in volume and eosinophilic, with relatively distinct cytoplasmic borders and prominent intercellular bridges. The mitotic rate was low, with only four mitoses observed in the eight available high-power fields. In areas, the epithelial surface was eroded and was associated with mild heterophilic and lymphocytic inflammatory cell infiltrates in both the neoplastic tissue and superficial dermis. The histologic findings confirmed a diagnosis of squamous cell carcinoma. The tumor extended approximately 250 μ m into the tissue samples that were examined, however, all the surgical margins (approximately 5 mm) were clear of tumor as assessed histologically.

Three months after surgery the iguana became anorexic and showed signs of lethargy. Blood was taken for analysis and showed a mild leukopaenia ($2.08 \times 10^9/L$; reference interval for *Iguana iguana* is $2.5 - 28.9 \times 10^9/L$), however haematocrit, uric acid, calcium and phosphate levels were all within reference ranges (Supplementary Table 1). Radiography revealed radiopaque shapes in the caudal abdomen. The iguana was subsequently anesthetized and exploratory ventralceliotomy performed, in which eggs were found and a diagnosis of follicular stasis was made, which is a common reproductive problem in captive female lizards.⁸ The eggs were removed and the iguana made a full recovery. At the time of surgery, no regrowth of the primary tumor, metastasis or abnormalities in relation to the

tumor were seen. At two years post-excision, although the iguana was not displaying any clinical symptoms, blood samples were taken and radiography was performed (using methods detailed above) to check for any signs of tumor re-growth or metastasis. The blood results were all within normal ranges (Supplementary Table 1) and no abnormalities or evidence of metastases were detected on the radiographs (Fig 3A-B). There was also no signs of re-growth of the primary mass, with only the scar from the surgical excision being visible (Fig 3C).

Discussion

SCCs are primarily found in the skin, subcutis, and oral cavity of affected reptiles, usually presenting as a visual mass if the lesion is on the skin or as inanition if the lesion is in the oral cavity.⁶ The tumors may present as a raised, proliferative lesion (varying from a firm plaque to a cauliflower-shaped lesion that is often ulcerated) or an erosive lesion (ranging from a shallow crusting lesion to a deep ulcer).⁹ The diagnosis is typically based on the histological characteristics of nests and infiltrative cords of poorly differentiated squamous cells, that can form central cores of compressed, laminated keratin (“keratin pearls”) or premature keratinization of individual cells (“dyskeratosis”).⁴ All of these features were observed in the case presented here.

SCC in reptiles commonly displays local invasion and metastatic spread is rare. To-date, case reports describing metastatic SCC have only been found in a diamondback rattlesnake (*Crotalus adamanteus*),¹⁰ a saltwater crocodile (*Crocodylus porosus*)¹¹ and two

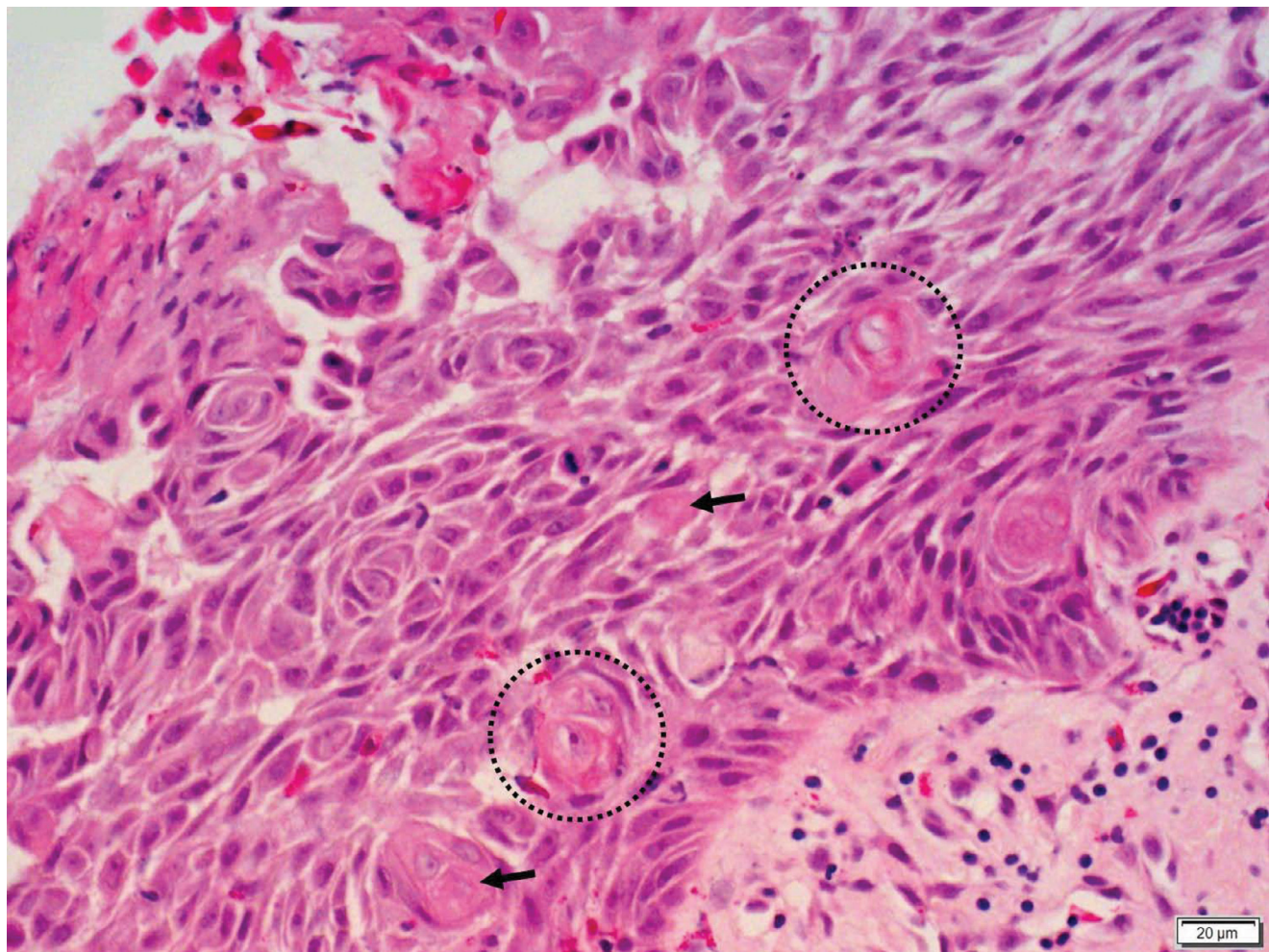


Fig 2. *Iguana iguana*, cutaneous squamous cell carcinoma. Multifocal dyskeratosis (arrows) and keratin pearl formation (dashed circles). H&E. Bar = 20 μ m.

loggerhead sea turtles (*Caretta caretta*).¹² The treatment options for SCC in dogs and cats typically include surgery and/or cryosurgery and radiotherapy, although other treatments have included photodynamic therapy, chemotherapy, or combination therapies.^{9, 13-14} In contrast, surgical excision remains the most commonly reported therapy for SCC in reptiles, with no recurrence if excision is complete.⁶ Our results are consistent with this finding, in that clear excision margins were achieved and at 2 years post-surgery there is no evidence of recurrence. Other successful treatments for reptiles with SCC have included photodynamic therapy (intravenous injection of chloro-aluminum sulfonated phthalocyanine 48 hours prior to irradiation with 675-nm light) for a South American boa constrictor (*Constrictor constrictor*)¹⁵ and surgery followed by electrochemotherapy (intratumoral administration of bleomycin followed by trains of biphasic electric pulses) in a yellow-bellied slider (*Trachemys scripta scripta*).¹⁶ In contrast, application of Imiquimod 5% cream (an immune response modifier) to a central bearded dragon (*Pogona vitticeps*)¹⁷ and radiation therapy (2 doses of 10Gy) on a Madagascar ground boa (*Acrantophis madagascariensis*)¹⁸ were not successful in controlling the tumor.

The cause of SCC in dogs and cats, similar to that for humans, is primarily to exposure to UV light, however, other risk factors include papillomavirus infection, environmental exposures (cigarette smoke and tobacco) and genetic predisposition.^{9, 13-14} In contrast, factors predisposing to tumor development in reptiles are not fully understood; genetic predisposition, hormone profile

alterations, viruses and solar radiation have all been suggested as possible factors.⁶ For example, papillomavirus DNA has been detected in a SCC from a Dumeril's boa (*Acrantophis dumerili*),¹⁹ and solar radiation may play a role, with artificial ultraviolet light exposure being implicated in a higher incidence of chromatophoromas in captive reptiles.²⁰ The green iguana in this case report lives in an indoor enclosure measuring 2.5 \times 2.5 \times 3 m³ with free access to a 125 watt Ultraviolet (UV) fluorescent bulb (Exo Terra, Montreal, Canada) and a 160 watt UV light bulb (Exo Terra) for nine hours per day, with one hour access to the outdoor enclosure depending on climatic conditions. During the summer months, she lives in a natural mesh enclosure for the entire period unless the temperature decreases below 19°Celsius.

Conclusion

This case report characterizes a rare cutaneous SCC affecting the flank of a green iguana. Histopathological analysis revealed an epidermal proliferation of neoplastic keratinocytes, with focal infiltration into the underlying superficial dermis. The tumor was surgically removed and there has been no sign of recurrence and/or any clinical symptoms 2 years later. This case report demonstrates that a differential diagnosis for a non-healing wound in lizards is cutaneous SCC, and that SCC may be successfully treated with surgical excision.

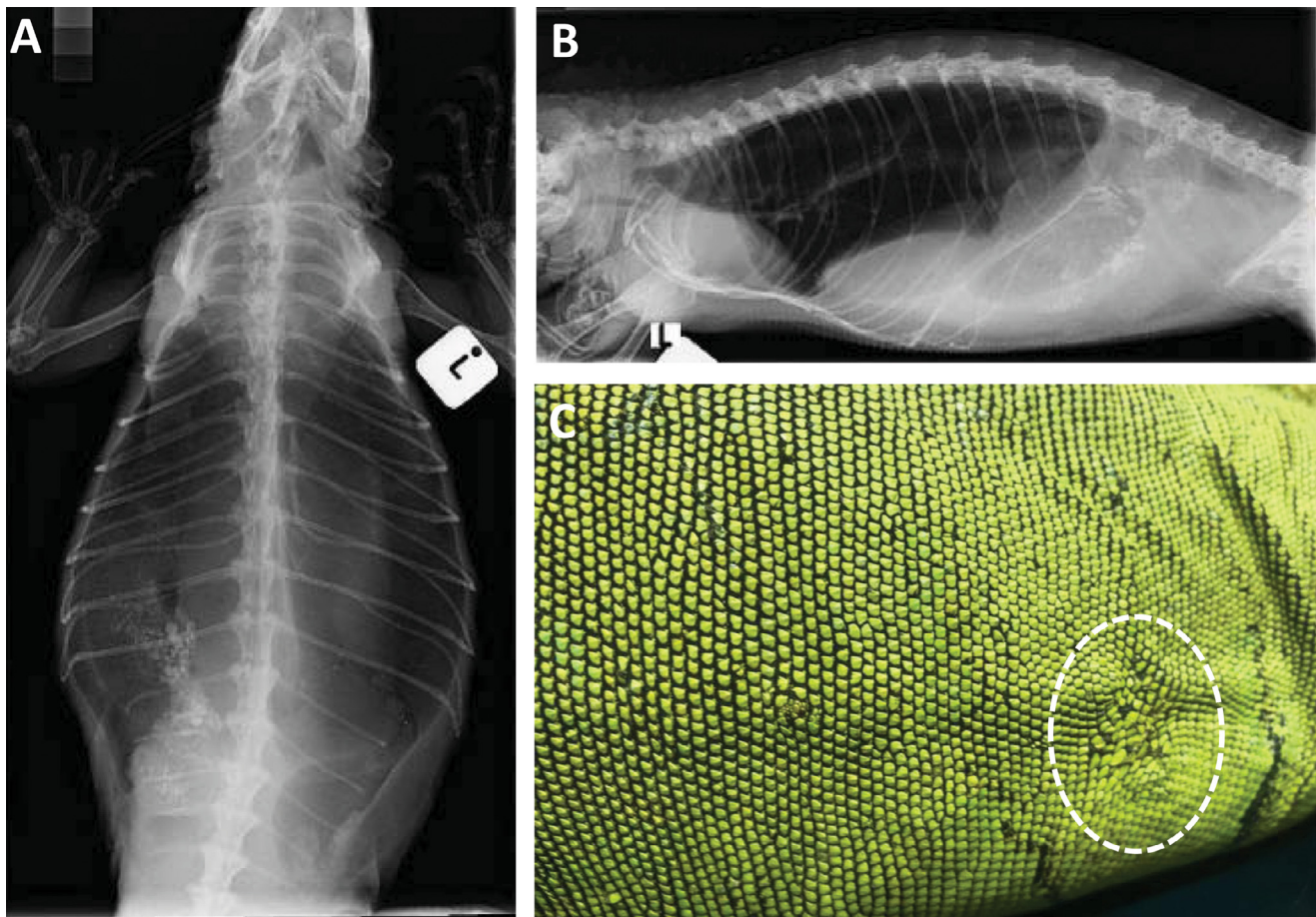


Fig 3. *Iguana iguana*, A 2 years after surgical removal of cutaneous squamous cell carcinoma. (A, B) Radiographs of the green iguana showing no abnormalities or evidence of metastases. (C) Photograph of the green iguana showing scarring at the site of the lesion (dashed circle) but no signs of recurrence of the tumor.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.tcam.2021.100610.

References

- Collis AH, Fenili RN. *The Modern US Reptile Industry*. LLC, Washington: Georgetown Economic Services; 2011
- Valdez JW. Using Google Trends to Determine Current, Past, and Future Trends in the Reptile Pet Trade. *Animals (Basel)* **11**:676, 2021
- Krysko KL, Enge KM, Donlan EM, Seitz JC. Distribution, Natural History, and Impacts of the Introduced Green Iguana in Florida. In: Gutman AJ, editor. *Iguana: Conservation, Natural History, and Husbandry of Reptiles*, International Reptile Conservation Foundation; 2007. p. 142–151
- Hernandez-Divers SM, Garner MM. Neoplasia of reptiles with an emphasis on lizards. *Vet Clin North Am Exot Anim Pract* **6**:251–273, 2004
- Sykes JM, Trupkiewicz JG. Reptile neoplasia at the Philadelphia Zoological Garden, 1901–2002. *J Zoo Wildl Med* **37**:11–19, 2006
- Christman J, Devau M, Wilson-Robles H, et al. Oncology of Reptiles: Diseases, Diagnosis, and Treatment. *Vet Clin North Am Exot Anim Pract* **20**:87–110, 2017
- Kubiak M, Denk D, Stidworthy MF. Retrospective review of neoplasms of captive lizards in the United Kingdom. *Vet Rec* **186**:28, 2020
- Knotek Z, Cermakova E, Oliveri M. Reproductive Medicine in Lizards. *Vet Clin North Am Exot Anim Pract* **20**:411–438, 2017
- Vail DM, Withrow SJ. Tumors of the skin and subcutaneous tissues D.M. (Eds.). In: Withrow SJ, editor. *Withrow and MacEwen's Small Animal Clinical Oncology*, St. Louis: Saunders Elsevier; 2007. p. 382–384
- Anderson ET, Kennedy-Stoskopf S, Sandy JR, Dorn B, Boyette T, Harms CA. Squamous cell carcinoma with vascular invasion in a diamondback rattlesnake (*Crotalus adamanteus*). *J Zoo Wildl Med* **41**:745–748, 2010
- Hill G, Dennis MM, Pyne M. Squamous cell carcinoma with hepatic metastasis in a saltwater crocodile (*Crocodylus porosus*). *Aust Vet J* **94**:83–86, 2016
- Orós J, Tucker S, Fernandez L, Jacobson ER. Metastatic squamous cell carcinoma in two loggerhead sea turtles *Caretta caretta*. *Dis Aquat Organ* **58**:245–250, 2004
- Liptak JM, Withrow SJ. Cancer of the gastrointestinal tract D.M. (Eds.). In: Withrow SJ, editor. *Withrow and MacEwen's Small Animal Clinical Oncology*, St. Louis: Saunders Elsevier; 2007. p. 456–472
- Miller PE, Dubielzig RR. Withrow and MacEwen's Small Animal Clinical Oncology. In: Withrow SJ, editor. *Ocular tumors*, St. Louis: Saunders Elsevier; 2007. p. 686–688
- Roberts WG, Klein MK, Loomis M, Weldy S, Berns MV. Photodynamic therapy of spontaneous cancers in felines, canines, and snakes with chloro-aluminum sulfonated phthalocyanine. *J Natl Cancer Inst* **83**:18–23, 1991
- Lanza A, Baldi A, Spugnini EP. Surgery and electrochemotherapy for the treatment of cutaneous squamous cell carcinoma in a yellow-bellied slider (*Trachemys scripta scripta*). *J Am Vet Med Assoc* **246**:455–457, 2015
- Pellett S, Pinborough M. Squamous cell carcinoma in a central bearded dragon (*Pogona vitticeps*). *Companion Anim* **19**:379–384, 2014
- Steil JC, Schumacher J, Hecht S, et al. Diagnosis and treatment of a pharyngeal squamous cell carcinoma in a Madagascar ground boa (*Boa madagascariensis*). *J Zoo Wildl Med* **44**:144–151, 2013
- Eleni C, Corteggio A, Altamura G, et al. Detection of Papillomavirus DNA in Cutaneous Squamous Cell Carcinoma and Multiple Papillomas in Captive Reptiles. *J Comp Pathol* **157**:23–26, 2017
- Heckers KO, Aupperle H. Pigment-forming tumors in reptiles: light regime and its dark sides. In: *Proceedings of the Association of Reptilian and Amphibian Veterinarians, 21th Annual Conference*, Orlando, Florida, USA: Association of Reptilian and Amphibian Veterinarians; 2014. p. 31–35