Possible Osteosarcoma Reported from a New World Elapid Snake and Review of Reptilian Bony Tumors

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Suggested running head: Elapid osteosarcoma

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ABSTRACT

Cancer chiefly occurs in vertebrates. Rare in amphibians, and perhaps common in reptiles, various neoplasms and malignant cancers have been reported with erratic frequency by museums, paleontologists, veterinarians, and pet hobbyists. Unsurprisingly, most herpetofaunal diversity has never been systematically surveyed for the presence of neoplasms owing to the extreme rarity or obscurity of many species. Museum collections can fill these gaps in knowledge, especially when researchers use non-destructive techniques. In this study, we used X-ray computed tomography to discover and characterize a possible osteosarcoma of the spine in a rare South American coralsnake, *Micrurus ancoralis*. Two spinal vertebrae were completely fused and adjacent vertebrae showed evidence of corruption. The fused vertebrae contained a hollow inner network thought to be vascular tissue. We also review previous reports of neoplasms in the Elapidae and all bony neoplasms in non-avian reptiles. The rarely reported technique of X-ray CT for tumor discovery could greatly improve our understanding of the species diversity and perhaps underlying causes of neoplasia.

Keywords: cancer, computed tomography, coralsnake, Elapidae, *Micrurus ancoralis*, neoplasm, osteopathy, tumor

Neoplasms, abnormal cell growths, can grow to large sizes and are often called tumors or cancers (Cooper, 1992; Hernadez-Divers and Garner, 2003). Tumors can be benign or malignant, and chiefly occur in vertebrates (Capasso, 2005). Neoplasms are reported across the entire spectrum of vertebrates (Schlumberger and Lucke, 1948; Stolk, 1958; Capasso, 2005; Rothschild et al., 2012). Amphibians rarely exhibit neoplasms (Capasso, 2005), though there are a few documented cases (Schlumberger and Lucke, 1948; Hill, 1954, 1955; Effron et al., 1977; Hruban, et al. 1992; Rothschild et al., 2012). In contrast, extant reptiles exhibit a diverse range of tumors (Machotka, 1984), and nearly all tumors found in mammals can be found in reptiles plus a few that can’t be found in mammals (Effron et al., 1977; Garner et al., 2004; Suedmeyer, 1995; Mauldin and Done, 2006; Rothschild et al., 2012). Our knowledge of reptilian neoplasms is primarily gleaned from systematic reviews from zoos (Hill, 1952–1955, 1957; Cowan, 1968; Ippen, 1972; Effron et al., 1977; Ramsay and Fowler, 1992; Ramsay and Lowenstein, 1996; Catão-Dias and Nichols, 1999; Sykes and Trupkiewicz, 2006), though important contributions have come from the pet trade and veterinary practice (Garner et al., 2004; Mader, 2005; Simard 2016; Christman et al., 2017), private collections (Frye, 1994), and museum collections (Harshbarger, 1969; Machotka and Whitney, 1980).

The frequency of tumors in vertebrates is unclear. A clear historical bias exists in the literature reflecting improved screening and expectations for what animals experience neoplastic growths, and only obvious cases were then reported (e.g., Ohlmacher, 1898; Kalin, 1937). For instance, Peyron (1939) dissected 4,000 snakes and reported no tumors. Similarly, Bergman

(1941) noted only one tumor in over 2,200 snakes. The occurrence of specific tumors also changes through time. As one example, Dawe and Harshbarger (1969) explain that reptiles lack leukemias, leukoses, or reticular neoplasms, yet Frye and Carney (1973) report a lymphatic leukemia in a boa constrictor only a few years later. In 1948, Schlumberger and Lucke presented an impressive review of fish tumors and commented on the state of tumor descriptions in vertebrates. They lamented that previous investigators did a rather poor job at surveying neoplasms in reptiles and this led to a misconception that reptilian neoplasms were rare or absent. Scrutinizing specimens with greater rigor clearly yielded a higher incidence of neoplasia than previously reported. For example, in the same paper they reported over 1,200 examples of renal adenocarcinoma in the frog *Rana pipiens* in a 15 year period (Schlumberger and Lucke, 1948).

One early effort to systematically report on vertebrate neoplasms was the annual report from the Zoological Society of London prosector (e.g., Hill 1952–1955, 1957). Here, all London Zoo causes of death were reported. These annual reports included unexpected tumors, thus raising the profile of neoplasms in non-mammals. Recognizing the paucity of data and importance of comparative information of neoplasms in animals, in 1969 the Smithsonian Institution established the Registry of Tumors in Lower Vertebrates (RTLA) to allow for a common repository to enhance study of such specimens (Harshbarger, 1969). The Armed Forces Institute of Pathology and the RTLA were critical in establishing the fact, now widely accepted, that tumors are widespread in vertebrates and are found in nearly all tissue types (Machotka and Whitney, 1980; Frye, 1994; Hernandez-Divers and Garner, 2003).

The question of neoplasm incidence or rate in vertebrates is still the subject of research and varies depending on the context of what incidence rate is being calculated. Among birds and mammals, neoplasms are apparently rare in wild populations, but far more likely in captive animals (Bergman, 1941; Petrak and Gilmore, 1982; Jubb and Kennedy, 1970; Capasso, 2005). Similarly, as previously reported, Bergman (1941) found only one tumor in 2,200 free-ranging snakes. Effron et al. (1977) provided one of the first modern, authoritative estimates of neoplasia in vertebrates from over 10,000 necropsies at the Zoological Society of San Diego. They reported a 3% rate of neoplasia in mammals and 2% in reptiles and birds. None of the amphibians dissected exhibited neoplasia. A more recent report from an exotic species pathology service hypothesized that, among reptiles, neoplasia may be most common in snakes (Garner et al., 2004). Garner et al. found that neoplasia in snakes are most prevalent in crotalids, followed by viperids, and then boids (including elapids [sic]). Simard (2016) recently reported 0.9% of 3995 reptiles available to Ghent University had some kind of neoplasm. Most cases were based on assessment of ante-mortem diagnostics; thus this estimate may be low since only very obvious neoplasms were reported. As reptiles are increasingly owned as pets (Collis and Fenili, 2011), systematic reports from the pet trade and associated veterinary profession will be crucial for expanding our knowledge of the incidence of tumors, at least in captive animals. However, this trend of neoplasm reporting will likely generate a bias towards those animals most commonly kept as pets. Thus, natural history collections will remain useful supplements to study neoplasia, especially in rare and 'uncharismatic' species not found in the pet trade (Keck et al., 2011).

In this report, we describe a pathology we think to be a bony, vascular tumor (osteosarcoma) of the new world elapid coralsnake, *Micrurus ancoralis* (Jan, 1872). Our discovery was made as part of a larger, systematic study of vertebral morphology in elapid snakes using computed tomography (CT). Prior to this report, we are unaware of any published neoplasms in new world elapid snakes (see Schmidt, 1936; Slowinsky, 1995 for phylogeny). Furthermore, our study is among the few published examples where CT has been used to find and describe a tumor in a vertebrate museum specimen (Chhem et al., 2006; Farke and O'Connor, 2007; Anné et al., 2015). Rosenberg et al. (1995), demonstrated difficult cases for describing osteosarcomas using plain radiographs and supplements known osteopathic cases with tomograms from CT. Schumacher and Toal (2001) enumerate radiography and ultrasonography techniques for reptile veterinary medicine but discount CT as a routine diagnostic tool. Banzato et al (2013a, b) review veterinary imaging for snakes and lizards and include traditional CT and contrast-enhanced in their review. Cole et al. (2014) used micro CT to describe osteosarcomas in mice injected with an osteosarcoma cell line, confirming that CT can accurately describe osteosarcoma without dissection. To demonstrate the rarity of this finding, we also review known elapid neoplasms and bony neoplasms in reptiles.

METHODS & MATERIALS

Computed Tomography

The formalin-fixed specimen was CT scanned at UT Arlintgon's Shimadzu Center for Environmental Forensics and Material Science using a Shimadzu inspeXio SMX-100CT (Shimadzu, Kyoto, Japan). The snake was scanned twice using similar parameters, but with different focal areas. Energy settings were 40kV and 40μA. All slices averaged 6 frames on each of 4 rotations for a total of 1200 views per full rotation. The first, focal scan consisted of 876 slices with 9 μm isotropic voxels. A second, multi-loop section with more vertebrae in focus consisted of 1697 slices with 11 μm isotropic voxels. Each scan lasted about 15 min.

Raw X-ray data were reconstructed using Shimadzu's inspeXio software and exported as 1024 x 1024 16-bit TIFF. Each stack of 16-bit TIFF images was rotated and cropped in ImageJ and imported into Thermo Scientific™ Avizo™ Software 9.5 (Thermo Fisher Scientific, Waltham, MA, US). As a volume, each data set was resampled to align better with the Z axis (center of the images), cropped, filtered using ring-artifact correction, passed through a non-local means filter, and then filtered using unsharp masking. This combination of filters retained fine features and smoothed the majority of artifacts found in all computed tomography data. Multiloop scans in cone beam CT inherently experience distortion at the periphery of each component scan, and this is slightly noticeable in the final, filtered data. Vertebrae were segmented in Avizo following Hall et al. (2018). In the multi-loop scan, pores in the fused vertebrae were segmented out using a combination of thresholding and manual editing. The raw

CT data, videos of each data set (Video 1-3), and label data are available on a MorphoSource project: http://www.morphosource.org/Detail/ProjectDetail/Show/project_id/625. Additionally, raw CT data are archived at the University of Texas at Arlington Amphibian and Reptile Diversity Research Center digital image collection.

Literature Reviews

We sought to generate two reviews of neoplasms in snakes: one specific to the snake family Elapidae, and another for all bony neoplasms in non-avian reptiles. We compiled a list of elapid neoplasms from a thorough literature search using relevant search terms in English, Spanish, German, French, and Dutch. This included searches with combinations of all genera of Elapid snake (reconciled between Campbell and Lamar [2004] and Uetz [2018]), the terms "elapid," "elapinae," or "Elapidae," and "tumor," "cancer," "neoplasm," or "sarcoma" etc. Similarly, we searched for bony tumors – defined as neoplasms of osteoids, periosteum, skeletal cartilage, and adjacent supporting tissues in the case of metastasis – in combination with common and scientific names for orders and family names of reptiles, per Uetz (2018). In each review, we examined all literature that cited relevant articles and also the references cited within. We did this regardless of whether these secondary articles could be found in the searches laid out above. Given the historical utility of the RTLA (e.g., Harshbarger, 1969), we contacted their current curatorial home to check for any unreported, relevant neoplasms for these reviews. For internal consistency, we updated common and scientific names throughout this report to match The Reptile Database (Uetz 2018).

RESULTS

Computed Tomography

Two cervical vertebrae were fused together in bone and vasculature (Fig. 1C,D; Video 1, 3). Fusion of the vertebrae increased from the ventral to dorsal aspect and will be described in this order. The centrum of fused vertebrae were mostly similar to unaffected vertebrae, except for additional vasculature in between adjacent condyle and cotyle. The hypapophysyes of fused vertebrae were not visibly different compared to unaffected vertebrae. The long haemal keel was also unchanged in the affected vertebrae. The lateral and subcentral foramina were unaffected. Dyapophyses were trabecular and apparently similar in affected and unaffected vertebrae. The paracotylar foramina were similar between unaffected and affected vertebrae. The neural canal was a similar size and shape between unaffected and affected vertebrae.

In contrast, the dorsal region of the fused two vertebrae was porous and resembled trabecular bone. Close inspection of the tomograms suggested that the porosity inside the pathological bones was generally vascular, rather than hollow. These canals, thought to be blood vessels, ran chaotically through each affected vertebra and seamlessly crossed the two vertebrae (Fig. 1D, Video 3). By contrast, blood vessels in unaffected bones only ran through the center of each lateral vertebral process, condyle, cotyle, and hypapophosis (Fig. 1B). No external anatomy seemed pathological to sight or touch.

The surface and interior of the neural arches were entirely fused between the two vertebrae and their surfaces were porous (Fig. 1C,D, Video 3). In contrast, the surface of cervical vertebrae elsewhere in the same specimen were smooth and not porous (Fig. 1A,B, Video 2). This changed the neural arches to appear more like the trabecular dyapophyses on the ventral and distal aspect of the vertebrae adjacent to articular ribs. The anterior aspect of the neural spine of the posteriorly adjacent vertebra was abnormally split in a Y-shape and porous (Video 1). The neural spines of the two anteriorly adjacent vertebrae were porous, dorsolaterally blunted, and enlarged on the anterior aspect (Video 1). The surface of the inside of the neural canal in fused vertebrae was rougher and thoroughly penetrated with vasculature compared to unaffected vertebrae.

Regarding the articulation between vertebrae, the condyle of the anterior fused vertebra and the adjacent cotyle were fused, with extra connecting vasculature (Fig. 1D). Similarly, the postzygaphyseal and prezygapophyseal articular facets of the affected vertebrae were fused with some porosity. The vasculature did not appear to connect the postzygaphyseal and prezygapophyseal articular facets (which is normal). Unaffected vertebrae exhibit a uniform gap here, but this gap was reduced in the affected vertebrae (Fig. 1, Video 1, 2). The zygosphene of the anterior fused vertebrae was completely merged with and indistinguishable from surrounding vascular bone from the posterior fused vertebrae (likely the zygantrum). Unlike the absence of vasculature connecting the postzygaphyseal and prezygapophyseal articular facets, we observed apparently complete vascular crossover where none is expected between the prezygapophysial articular facet and postzygapophysial articular facet, zygosphene and zygantrum, and adjacent neural spines (Fig. 1, Video 3). The intrazygantral foramina of fused vertebrae were not obviously distinguished from the abnormal vasculature and bone. There was a slight asymmetry to remaining cartilage thickness in affected articular facets (Fig. 1D, Video 3) compared to symmetrical cartilage thickness between these joints in unaffected vertebrae (Fig. 1B, Video 2).

Literature Reviews

We found 38 cases of neoplasia in the snake family Elapidae, all from old world species (Table 1). Of 13 cases when sex was reported, four were male and nine were female. Twenty-three (60%) cases reported were from the genus *Naja*, followed by *Aspidelaps* (4; 10.5%) and *Ophiophagus* (3, 7.9%). Kidney-related neoplasms were the most reported (9, 23.7%; Keck et al. 2011). Despite the limited number of reported elapid neoplasms, reports covered many cell types and locations (Table 1), including three bony tumors in *Naja* species. Our review of bony tumors in reptiles revealed 58 cases (Table 2). This included 49 squamates, 5 turtles, and 4 crocodylians. Six of ten cases with known sex were female and four were male. We found several varieties of bony neoplasms, including osteoma (bone cell neoplasm), osteosarcoma (malignant bone cell tumor), osteochondroma (bony, cartilage covered exostoses), chondroma (cartilage cell neoplasm), and chondrosarcoma (malignant cartilage cell tumor). *Varanus* and *Pantherophis* each included eight cases of bony tumors (16.3% of squamates). We note very few bony tumors of the head or face: only one report of osteoma of the skull from a male *Caiman crocodilus* (Kalin 1937).

Currently, the RTLA resides at Experimental Pathology Laboratories in Virginia. Jeffrey Wolf, current curator of the RTLA, knew of only one bony tumor in the Elapidae from their collection: a metastatic vertebral osteochondrosarcoma in *Naja nigricolis* (RTLA case #2474). Wolf noted no tumors in the collection within the genus *Micrurus*. Additionally, Wolf reported the following elapid neoplasms in the RTLA archive: six renal adenocarcinomas, two hepatocarcinomas, two lymphomas, one fibrosarcoma, one nasal carcinoma, one leiomyosarcoma, one Sertoli cell tumor, and one adrenal adenoma.

DISCUSSION

There are few possible explanations for the displayed osteopathy: 1) osteoperiostitis (bone inflammation), 2) osteomyelitis (bone infection), or 3) neoplasm (abnormal cell growth). There is a precedent for osteoperiostitis in two female Black Iguanas (*Ctenosaura similis*) and a female Chinese Stripe-tailed Snake (*Elaphe taenura*; Cowan, 1968). In each case, the bone and adjacent soft tissue became indistinct, softened, and exhibited exostosis. The periosteum of the laminae was affected, but not the intervertebral or apophyseal joints. Microscopically, the periosteum separated the new growth from the original bone, as new growth arose from the mesenchymal tissue on the surface of the periosteum. Cowan (1968) compared these three osteopathic growths to virally induced osteoperiostitis (i.e., osteopetrosis) in chickens (Sanger et al., 1966). Compared to osteoperiostitis, as reported by Cowan (1968), the specimen in the current study had fused intervertebral (i.e., condyle and cotyle; zygosphene and zygantrum) and apophyseal joints. The scarcity of the elapid specimen led the respective curator to disallow destructive histopathology. This prevents us from ruling out, at present time, microscopic growth on the periosteum. From the radiology presented here, though, it seems the growth occurred inside of existing bone and not on top of the periosteum. For example, the vasculature perfusing the neural crest seems unlikely to progress etiologically from growth on the periosteum. In the absence of compelling evidence to suggest otherwise, we thus rule out osteoperiostitis for UTA R-55945.

An alternative is the possibility of infection of the bone or its supporting tissues (Rothschild et al., 2012). Rothschild and colleagues exhaustively review and in some cases re-evaluate osteopathological conditions reported in the herpetological literature and rule several cases to be due to bone infection (Rothschild et al., 2012). In our study, infection cannot be ruled out, but there is clear evidence for neoplastic growth: low anisotropy of the bone, fused bones, and absence of bony growth on and in the periosteum. Comparative histopathology of similar snake pathologies with known underlying causes would resolve this most compelling alternative explanation. In the absence of firm data on the anatomy of bone infection in elapid snakes, the ideal follow up experiment might induce infection in a limited number of animals for later post mortem examination.

The remaining explanation, a type of neoplasia, overlaps with many of our observations. There was, of course, alteration of bone, as is seen in other bony tumors. The blunted and bloated neural crests and dorsal centrum were perfuse with vasculature. For this reason, we distinguish the neoplasia to be a tumor, and a tumor not restricted to one cell type (i.e., malignant). From radiology presented here, it is not possible to precisely list cell type that was affected by the tumor, but it does appear to originate from the bone tissue itself, etiologically. That would narrow the type of neoplasia to an osteosarcoma, or malignant bone cell tumor. Again, we admit that our evidence for this diagnosis is not infallible as we base our determination off of one specimen and using only one non-destructive technology.

Tumor vasculature becomes interesting in our study since we could easily segment it from the specimen's micro CT data (Figure 1B,D). Generally speaking, solid tumors are more vascularized than healthy tissues (Forster et al., 2017), but their chaotic growth results in chronic and acute hypoxia due to poor circulation (Siemann, 2011; Forster et al., 2017). Among the earliest comments on vasculature of bony tumors in reptiles is Hill's (1957) report of a vascular osteoid osteoma in a Common Water Monitor (*Varanus salvator*). Hill (1957) briefly notes that reptile osteomas (at least in snakes) may be synonymous with exostoses found in human osteomas. Interestingly, Stolk (1958) reports several osteomas in the caudal vertebrae of a female European Green Lizard (*Lacerta viridis*) that exhibited normal vasculature. The discrepancy in vasculature may be due to a different origin for the neoplastic growth in the *Lacerta*, as Stolk (1958) hypothesized the tumors to have originated from the marrow of the caudal long bones. Fitting with the generally chaotic nature of tumor vasculature, Cowan et al. (2011) reported an osteosarcoma in a Woma Python (*Aspidites ramsayi*) that was characterized by disorderly arrangement of osseous trabeculae. They also noted that mesenchymal cells surrounded an eosinophilic osteoid matrix.

Looking backwards through time, bony tumors do occasionally show up in the reptile fossil record (Moodie, 1917, 1923). A well-known example is Moodie's (1918) description of an osteoma in a mosasaur (see also Moodie, 1923). In this case, however, Rothschild et al. (2012) reassessed this paleontological osteopathy as a hamartoma (i.e., not considered neoplasia). Our review also includes bony neoplasms in an extinct turtle, *Syllomus aegyptiacus* (Weems, 1974), and an extinct crocodile, *Leidyosuchus formidabilis* (Sawyer and Erickson, 1998), though these two examples are archosaurs and not lepidosaurs. The fossil record is sparse and uneven across time, and the condition and taphonomy of fossils complicates their accurate osteopathological diagnosis (Moodie, 1917; Rothschild et al., 2012). Computed tomography, especially from a synchrotron light source, may assist properly diagnosing suspected fossil neoplasms, as histology is typically ruled out.

Prior to our report, we are unaware of any published neoplasms in new world elapid snakes (Table 1), likely reflecting their general absence in private collections and zoos compared to other species (Keck et al., 2011). Large, charismatic venomous cobras of the old world are relatively common in zoos throughout the world (e.g., Ramsay et al., 1996; Catão-Dias and Nichols, 1999; Collis and Fenili, 2011) and would thus be expected to be necropsied more often (Table 1). Compared to the hundreds of tumors reported for other families of snakes (Garner et al. 2004), even the RTLA (similar to other collections and reports), likely reflects the historical bias against including elapid snakes in zoo and private collections (Keck et al., 2011; Wolf J, pers. comm.), as they are highly venomous. The relative obscurity of new world elapids (Schmidt, 1936), especially in captivity (Collis and Fenili, 2011), thus requires focused effort investigating specimens in natural history collections, to find their neoplasms. Another obvious omission in the neoplasm literature is a comparative phylogenetic study of tumors across reptiles and birds. Machotka and Jacobson (1989) provided the most recent phylogenetically organized treatment of neoplasms in reptiles; however, this study was entirely descriptive. Furthermore, our knowledge of comparative phylogenetics (e.g., Freckleton et al., 2002) and the reptile phylogeny has since vastly improved (Reeder et al. 2015, Streicher and Wiens, 2017). A comparative phylogenetic test of neoplasia prevalence across the Sauria would reveal unexpected neoplasm absences and focus future study of natural history collections on these groups. Our report demonstrates that studying neoplasms is sometimes possible without dissecting valuable, rare specimens.

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FIGURE LEGENDS

Figure 1. Vertebral osteosarcoma in a new world elapid snake, *Micrurus ancoralis* (UTA R-55945). Pairs of vertebrae from unaffected (A, B) and pathologic (C, D) regions of the spine as shown with micro-computed tomography. Blood vessels (in red) and ligament and cartilage (in blue) are shown (B and D) for each pair. Chaotic vasculature is shown in green for pathologic vertebrae (D). From left to right, views are cranial, caudal, dorsal, ventral, and both lateral angles. Scale bars are 1 mm.

Video 1. Section of vertebrae surrounding a vertebral osteosarcoma in *Micrurus ancoralis* (UTA R-55945). Available from MorphoSource: http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34110.

Video 2. Pair of normal vertebrae in *Micrurus ancoralis* (UTA R-55945). Blood vessels are shown in red and connective tissues are shown in blue. Available from MorphoSource: http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34108.

Video 3. Fused pair of pathologic vertebrae in *Micrurus ancoralis* (UTA R-55945). Blood vessels are shown in red, chaotic vasculature is shown in green, and connective tissues are shown in blue. Note the blunted and nearly absent neural spine and indistinguishable nature of the two vertebrae. Available from MorphoSource:

http://www.morphosource.org/Detail/MediaDetail/Show/media_id/34109.

Table 1. Neoplasms found in the snake family Elapidae.

Scientific Name	Common Name	Neoplasm	Reference
Acanthophis antarcticus ♀	Common Death Adder	Lymphosarcoma, leukemic	Effron et al., 1977
Aspidelaps l. lubricus	Cape coral snake	Tubular carcinoma (kidney)	Keck et al., 2011 (unpublished)
Aspidelaps l. lubricus ♀	Cape Coral Snake	Renal adenocarcinoma	Keck et al., 2011
Aspidelaps l. lubricus ♀	Cape coral snake	Renal adenocarcinoma	Keck et al., 2011
Aspidelaps l. lubricus ♂	Cape Coral Snake	Renal adenocarcinoma	Keck et al., 2011
Acanthophis madagascarensis (92-SnN-75)*	??	Squamous cell carcinoma	Frye, 1994
Dendroaspis polylepis	Black Mamba	Biliary adenocarcinoma with sarcomatous desmoplasia	Ramsay et al., 1996
Naja atra	Chinese Cobra	Carcinoma (pancreas?)	Machotka and Whitney, 1980
Naja haje (87-B-51)	Egyptian cobra	Papillary adenoma	Frye, 1994
Naja melanoleuca	Black-and-white Cobra	Venom gland carcinoma	Hill, 1952
Naja melanoleuca	Black Cobra	Osteochondrosarcoma (spinal column)	Wadsworth, 1954a, b
Naja melanoleuca (?)	"African Black Cobra"	Osteochondroma (dorsal aspect of spinal column)	Wadsworth, 1954b
Naja melanoleuca ♂	Black Cobra	Ductular adenocarcinoma (pancreas)	Sykes and Trupkiewicz, 2006
Naja naja	Indian Cobra	Biliary adenoma	Ramsay et al., 1996
Naja naja	Indian Cobra	Renal adenoma	Ramsay et al., 1996
Naja naja	Indian Cobra	Adrenal adenoma	Ramsay et al., 1996
Naja naja	Indian Cobra	Bile duct adenoma	Cowan, 1968
Naja naja	Indian Cobra	Ganulosa cell tumor	Ramsay et al., 1996
Naja naja	Indian Cobra	Pancreatic carcinoma	??
Naja naja	Indian Cobra	Granuloma (head and neck)	Wadsworth, 1956

Naja naja (80-68452)	Indian Cobra	Seminoma	Frye, 1994
Naja naja (RTLA 560)	Indian Cobra	Leiomyosarcoma	Machotka and Whitney, 1980
Naja naja ♀	Indian Cobra	Hepatocellular carcinoma (liver)	Catão-Dias and Nichols, 1999
Naja naja ♀	Indian Cobra	Hepatocellular carcinoma (liver)	Catão-Dias and Nichols, 1999
Naja nigricollis (90-SB-63)	Black-necked Spitting Cobra	Renal, Tubular adenoma	Frye, 1994
Naja nigricollis ♀	Black-necked Spitting Cobra	Lymphosarcoma	Effron et al., 1977
Naja nigricollis ♂	Black-necked Spitting Cobra	Bile duct adenoma	Cowan, 1968
Naja nigrigollis	Black-necked Spitting Cobra	Osteochondrosarcoma (Metastatic to Spleen and Kidney)	Machotka and Jacobson, 1989
Naja nivea ♂	Cape Cobra	Bronchogenic adenocarcinoma	Effron et al., 1977
Naja sp. (93-SnN-82)	Cobra	Hepatoma, malignant	Frye, 1994
Naja sp. (*haje?*)	Egyptian cobra	Lynphosarcoma (heart and liver)	Cowan, 1968
Ophiophagus hannah	King Cobra	Lymphoma	Willette et al., 2001
Ophiophagus hannah ♀	King Cobra	Tubular adenoma (kidney)	Catão-Dias and Nichols, 1999
Ophiophagus hannah ♀	King Cobra	Chondrosarcoma (vertebra)	Vico et al., 2016
Pseudechis porphyriacus ♀	Red-bellied Black Snake	Papillomas of skin; adenomatous proliferation of intrahepatic bile ducts	Effron et al., 1977
Pseudechis sp.	Black Snake	Fibrosarcoma	Wadsworth, 1956
Walterinnesia aegyptia	Sinai Desert Cobra	Renal adenocarcinoma	Frye, 1991a
Walterinnesia sp. (88-N-01)	Black Desert Cobra	Renal tubular adenoma	Frye, 1994
"Elapid"	Cobra (?)	Adenocarcinoma (Pancreas)	Ratcliffe, 1943

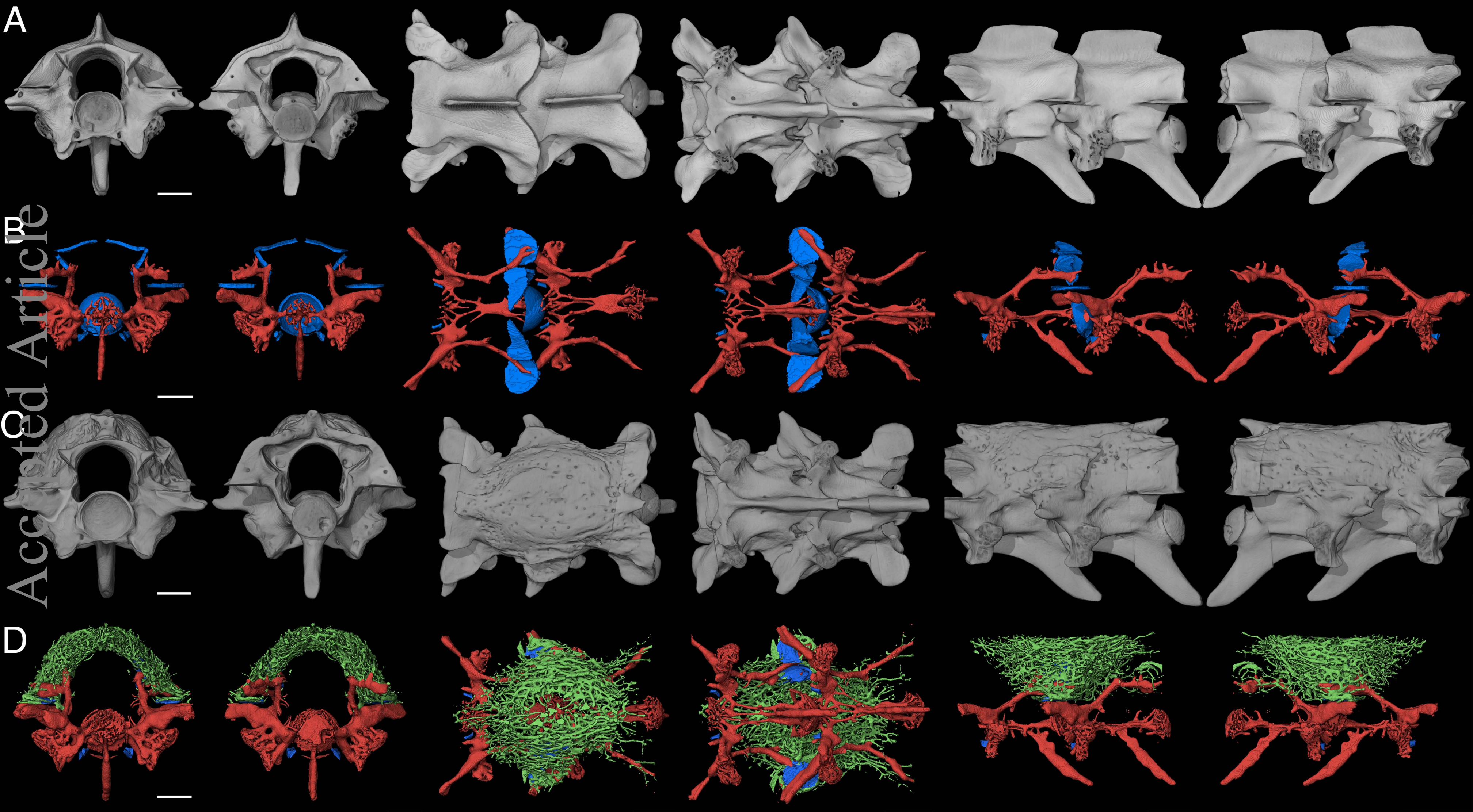
[1]Possibly *Acrantophis madagascariensis*, which is not an Elapid.

Table 2. Summary of bony neosplasms reported in non-avian reptiles.

Scientific name	Common name	Neoplasm	Reference
Squamata			
Aspidites ramsayi	Woma Python	Osteosarcoma	Cowan et al., 2011
Colubrid sp. (5)	-	Chondrosarcoma	Garner et al., 2004
Crotalid sp.	-	Osteosarcoma (vertebra)	Garner et al., 2004
Crotalid sp. (2)	-	Chondrosarcoma	Garner et al., 2004
Crotalus ruber (RTLA 984)	Red Diamond Rattlesnake	Undifferentiated sarcoma (dorsal and lateral to spinal column)	Harshbarger, 1975 (contributed by E. A. Holzinger)
Cyclura cornuta	Rhinoceros Iguana	Chondro-osteofibroma	Jacobson, 1981, Machotka, 1984
Cyclura cornuta	Rhinocerus Iguana	Osteochondrosarcoma, fibrosarcoma (legs and pelvis)	Rodhain, 1949
Cyclura cornuta	Rhinocerus Iguana	Osteochondrosarcoma, fibrosarcoma (pelvis)	Rodhain, 1949
Cyclura nebula	Cuban Lizard	Osteochondroma (humerus, femur, other)	Ippen, 1966
Dendroaspis polylepis	Black Mamba	Osteochondrosarcoma	Wadsworth, 1954a, b
Elapid sp.	Cobra (?)	Osteosarcoma (extraskeletal)	Garner et al., 2004
Gekko gecko	Tokay Gecko	Mineralized carcinoma in endolymphatic sac	Sander et al., 2015
Gerrhosaurus sp.	Plated Lizard	Chondrosarcoma (humerus)	Garner et al., 2004
Iguana igauna ♀	Common Green Iguana	Osteosarcoma	Dietz et al., 2015
Iguana iguana	Common Green Iguana	Osteochondroma (legs)	Ippen, 1966
Iguana iguana ♀	Common Green Iguana	Osteosarcoma (fibroblastic)	Dietz et al., 2015
Lacerta viridis	Emerald Lizard	Osteosarcoma (multiple)	Jacobson, 1981
Lacerta viridis ♀	European Green Lizard	Osteomas (tail vertebrae)	Stolk, 1958
Naja melanoleuca	African Black Cobra	Osteochondrosarcoma (spinal column)	Wadsworth, 1954b
Pantherophis guttatus	Corn Snake	Chondrosarcoma (mandible)	Schmidt and Reavill, 2012

Pantherophis guttatus	Corn Snake	Chondrosarcoma	Mauldin and Done, 2006
Pantherophis guttatus	Corn Snake	Chondrosarcoma (vertebra)	Dawe et al., 1980
Pantherophis guttatus	Corn Snake	Chondrosarcoma (vertebra)	Garner and Collins, 1995
Pantherophis guttatus	Corn Snake	Chondrosarcoma	Hoff et al., 1984
Pantherophis guttatus	Corn snake	Chondrosarcoma	Harshbarger, 1974
Pantherophis guttatus ♀	Corn snake	Osteosarcoma (ribs)	Simard, 2016
Pantherophis obsoletus	Black Rat Snake	Undifferentiated sarcoma with osseous metaplasia (Abdominal cavity and liver)	Machotka and Whitney, 1980 (contributed by R. S. Wilhelm)
Pantherophis obsoletus obsoletus	Western Rat Snake	Chondrosarcoma (vertebra)	Honour et al., 1993
Pogona vitticeps	Central Bearded Dragon	Osteosarcoma (fibroblastic)	Dietz et al., 2015
Python bivittatus	Burmese python	Osteosarcoma (mandible)	Frye, 1991a
Rhamphiophis rostratus	Rufous-beaked Snake	Osteosarcoma (spine)	Hill, 1955
Uromastyx dispar maliensis	Sudan Mastigure	Periosteal chondroma (juxtacortical bone)	Gál et al., 2007
Varanus acanthurus ♂	Spiny-tailed Monitor Lizard	Chondroblastic osteosarcoma	Needle et al., 2013
Varanus acanthurus ♂	Spiny-tailed Monitor Lizard	Chondroblastic osteosarcoma	Needle et al., 2013
Varanus bengalensis	Bengal Monitor	Osteochondroma (neck)	Frye, 1991b
Varanus bengalensis nebulosus (juv.)	Bengal Monitor	Osteocartilaginous exotoses	Frye, 1991a
Varanus dracoena	Indian Monitor	Enchondroma (multiple bones)	Bland-Sutton, 1885
Varanus griseus	Desert Monitor Lizard	Osteochondrosarcoma	Schönbauer et al., 1982
Varanus salvator	Common Water Monitor	Chondromatous enlargement on hyoid	Hill, 1957
Varanus salvator ♀	Common Water Monitor	Osteoid osteoma (vascular)	Hill, 1957
Viperid sp.	-	Osteosarcoma (vertebra)	Garner et al., 2004
Viperid sp. (2)	-	Chondrosarcoma	Garner et al., 2004
?	"Lizard"	Chondrosarcoma	Hernandez-Divers and Garner, 2003

?	“Unidentified snake”	Osseous metaplasia (Subcutis)	Ramsay et al., 1996
Chelonia			
Chelonoidis sp. (TAMU 219609)	Galapagos Tortoise	Osteoma	Christman et al., 2017
Cyclemys dentata	Asian Leaf Turtle	Adenocarcinoma (femur)	Gál et al., 2010
Gopherus agassizii	California Desert Tortoise	Chondroma (carapace)	Rosskopf, 1986
Pseudemys rubriventris ♀	Northern red-bellied turtle	Mucinous melanophoroma (humerus)	Bielli et al., 2015
Syllomus aegyptiacus	[Extinct species]	Osteoma (or osteoblastoma)	Weems, 1974; Rothschild et al., 2013
Crocodylia			
Caiman crocodilus ♂	Spectacled Caiman	Osteosarcoma (vertebra)	Kalin, 1937
Caiman crocodilus ♂	Spectacled Caiman	Osteoma (skull, shoulder)	Kalin, 1937
Crocodylus porosus ♀	Saltwater Crocodile	Osteoma and osteosarcoma (hands and radius)	Kalin, 1937
Leidyosuchus (=*Borealosuchus*) *formidabilis*	[Extinct species]	Osteoma, chondroma	Sawyer and Erickson, 1998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