

# UC Davis

## UC Davis Previously Published Works

### Title

Alimentary squamous cell carcinoma in psittacines: 12 cases and review of the literature

### Permalink

<https://escholarship.org/uc/item/54h1z8hg>

### Journal

Journal of Veterinary Diagnostic Investigation, 33(5)

### ISSN

1040-6387

### Authors

Gonzalez-Astudillo, Viviana  
Mete, Asli  
Navarro, Mauricio A  
et al.

### Publication Date

2021-09-01

### DOI

10.1177/10406387211021480

Peer reviewed

# Alimentary squamous cell carcinoma in psittacines: 12 cases and review of the literature

Viviana Gonzalez-Astudillo,<sup>1</sup> Asli Mete,<sup>1</sup> Mauricio A. Navarro,<sup>1</sup> Francisco A. Uzal,<sup>1</sup> Javier Asin<sup>1</sup>

**Abstract.** Squamous cell carcinoma (SCC), which is a neoplasm that usually arises from the integument, is reported uncommonly in pet birds. Only a few reports of SCCs in the alimentary tract of birds, including psittacines, have been published, and a detailed description of the pathology is not available in the literature. We present here 12 cases of alimentary SCC in psittacines. The average age of the birds was 22.2 y (range: 15–29 y), and affected species included 4 Amazon parrots (*Amazona* sp.), 3 cockatiels (*Nymphicus hollandicus*), 3 macaws (*Ara* sp.), 1 conure (*Eupsittula* sp.), and 1 Senegal parrot (*Poicephalus* sp.). Frequent clinical complaints included regurgitation, dysphagia, dyspnea, lethargy, and/or weight loss. SCC primarily affected the oral cavity in 6 of 12 cases, the crop alone in 2 of 12 cases, the crop and esophagus in 1 of 12 cases, the proventriculus alone in 1 of 12 cases, and the crop, esophagus, and proventriculus in 2 of 12 cases. Histologically, alimentary SCCs were locally invasive and often resulted in mucosal ulceration. Although there were no metastases in any of our cases, poor clinical outcomes were frequent and associated most commonly with complete effacement of the alimentary segment and severe inflammation with opportunistic bacterial infection. Our review of the literature records commonly affected species, variability of gross presentations and clinical signs, plausible etiologies, and current diagnostic developments.

**Keywords:** alimentary neoplasia; psittacines; squamous cell carcinoma.

Squamous cell carcinomas (SCCs) are reported uncommonly in pet birds, with only a few cases documented in a variety of avian taxa, including psittacines.<sup>1,3,5,8,9,15,25,37</sup> The majority of documented cases of SCCs in psittacines occurred in parrots (*Amazona* sp.), cockatiels (*Nymphicus* sp.), and budgerigars (*Melopsittacus* sp.), followed by conures (subfamily Arinae), cockatoos (*Cacatua* sp.), African grey and eclectus parrots (*Psittacus erithacus* and *Eclectus roratus*, respectively), and macaws (*Ara* sp.).<sup>1–4,6,7,9,12–16</sup> SCCs in birds can occur in any location, typically in rostral mucocutaneous junctions, uropygial gland, choana, distal wing (phalanges and patagium) and, less commonly, the alimentary tract.<sup>3,9,10,19,26</sup> Compared to their integumentary counterparts, alimentary SCCs are poorly studied in terms of specific location, gross and histopathologic features. We present here a retrospective study of 12 alimentary SCCs in psittacines and a review of the literature.

## Materials and methods

We searched the database of the California Animal Health and Food Safety Laboratory System (CAHFS) to identify laboratory or field autopsy and biopsy cases of psittacines with a diagnosis of SCC, from January 1, 1990, through June 24, 2020. Inclusion criteria for our study were 1) psittacine carcasses or tissues submitted for gross and histologic

examination, and 2) a diagnosis of SCC in any part of the alimentary system. The final report for each case was reviewed, and the signalment, clinical history, manner of death, and gross and histologic findings were recorded.

For histopathology, hematoxylin and eosin (H&E)-stained slides were retrieved from the archives, or recuts were obtained from 10% formalin-fixed, paraffin-embedded tissues. Although tissues sampled varied on a case-by-case basis, laboratory and field autopsies generally included sections of the neoplasm, brain, peripheral nerves, heart, trachea, larynx, air sacs, thyroid glands, lung, liver, esophagus, crop, proventriculus, ventriculus, pancreas, intestines, spleen, kidneys, gonads, and skeletal muscle. Biopsies included the neoplasm and associated tissues. All tissues were fixed in 10% neutral-buffered formalin for 24–72 h and processed routinely to produce 4- $\mu$ m-thick H&E-stained sections. For carcasses with oral SCCs, samples of the head were demineralized by immersion in a commercial fixative/demineralizing solution for several days, before routine

California Animal Health and Food Safety Laboratory, San Bernardino (Gonzalez-Astudillo, Navarro, Uzal, Asin) and Davis (Mete) branches, University of California–Davis, Davis, CA, USA.

<sup>1</sup>Corresponding author: Javier Asin, California Animal Health and Food Safety Laboratory, University of California–Davis, 105 W Central Ave, San Bernardino, CA 92408, USA. [jasinros@ucdavis.edu](mailto:jasinros@ucdavis.edu)

**Table 1.** Demographics, taxonomic distribution, clinical history, and type of death of psittacines diagnosed with squamous cell carcinoma in different locations of the alimentary tract.

Case	Common name	Scientific name	Age (y)	Sex	Type of death	History
1 <sup>LA</sup>	Cockatiel	<i>Nymphicus hollandicus</i>	23	M	E	1-wk dyspnea
2 <sup>LA</sup>	Cockatiel	<i>Nymphicus hollandicus</i>	15	F	S	Regurgitation, weight loss
3 <sup>FA</sup>	Cockatiel	<i>Nymphicus hollandicus</i>	Adult	F	S	Failed treatment of oral mass
4 <sup>FA</sup>	Amazon	<i>Amazona finschi</i>	28	M	S	Regurgitation, weight loss
5 <sup>LA</sup>	Amazon	<i>Amazona auropalliata</i>	25	M	S	Found dead
6 <sup>B</sup>	Amazon	<i>Amazona ochrocephala</i>	27	U	U	Not provided
7 <sup>LA</sup>	Amazon	<i>Amazona</i> sp.	Adult	M	U	Not provided
8 <sup>LA</sup>	Macaw	<i>Ara severus</i>	29	M	E	Weight loss, neurologic and respiratory signs
9 <sup>LA</sup>	Macaw	<i>Ara chloropterus</i>	Adult	F	S	Found dead
10 <sup>B</sup>	Macaw	<i>Ara chloropterus</i>	25	F	U	Not provided
11 <sup>LA</sup>	Parrot	<i>Poicephalus senegalus</i>	11	F	S	Weight loss, acute listlessness
12 <sup>LA</sup>	Conure	<i>Eupsittula aurea</i>	17	U	U	Not provided

B = biopsy; E = euthanasia; F = female; FA = field autopsy; LA = laboratory autopsy; M = male; S = spontaneous; U = unknown.

histologic processing. All slides that included the SCCs were re-examined by one of the authors (J. Asin) to provide a uniform descriptive and systematic analysis of the histologic findings. On each slide, mitoses were counted in 10 contiguous high-power fields (HPF) to obtain a mitotic count (MC) in 2.37 mm<sup>2</sup>. In addition, neoplastic cell arrangement, keratin pearls, fibroplasia or fibrosis (interpreted as desmoplastic response or as granulation tissue), and necrosis and/or ulceration were evaluated.

Additional testing was carried out following CAHFS standard operating procedures and varied depending on the clinical history, client requests, gross findings, and/or the pathologist's criteria. These included: aerobic, anaerobic, and fungal culture of liver, lung, kidney, cloaca, and neoplastic tissue (nasal cavity, crop, esophagus, proventriculus); *Salmonella* spp. culture of liver, lung, intestines, and/or neoplastic tissue; avian influenza A virus and virulent Newcastle disease virus (*Avian orthoavulavirus 1*) PCR on pharyngeal and cloacal swabs; periodic acid-Schiff (PAS) and Gram stains of selected sections; immunohistochemistry for avian bornavirus (genus *Orthobornavirus*) on proventriculus and brain; *Chlamydia* sp. fluorescent antibody test (FAT) on liver, air sac, and spleen smears; heavy metal screen (including arsenic, cadmium, copper, iron, lead, manganese, mercury, molybdenum, zinc) and selenium concentrations in liver and/or kidney; vitamin A and E concentrations in liver; and fecal flotation parasitologic tests.

## Results

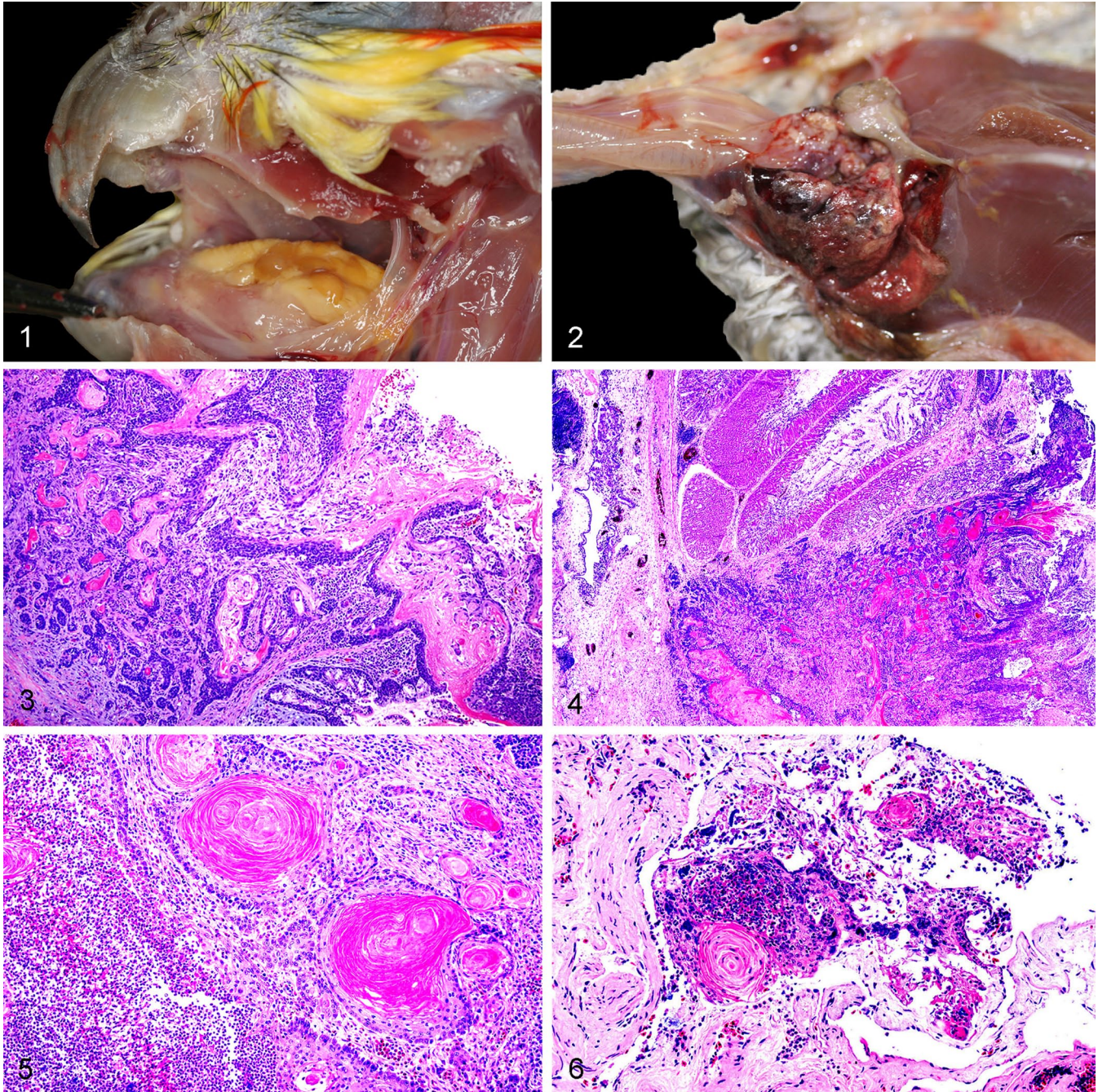
We found 12 cases of psittacines with SCC in different areas of the alimentary tract in the CAHFS database. Specifically, 8 were autopsied in CAHFS laboratories, 2 in the field, and 2 cases were biopsy specimens (Table 1).

The oral cavity was the most frequently affected segment (6 of 12 cases), and for those with available gross descriptions, neoplasms in that area were: 1) light-yellow, multilobulated,

cauliflower-like masses arising from the hard palate (case 9), 2) prominent mats mimicking caseous exudate (case 12), or 3) yellow lobular material replacing and expanding the glossal mucosa and extending to the pharyngeal region (case 1; Fig. 1). No additional gross descriptions, except that they were located in the oral cavity and choana, were available for biopsy cases 6 and 10, or for field autopsy case 3.

The crop was the second most frequently affected segment (5 of 12 cases), either alone (cases 2, 11) or also affecting the esophagus (case 5), or both the esophagus and the proventriculus (cases 7, 8). SCCs affecting the crop and associated organs were described as a hemorrhagic, tan, and friable mass filling the crop and esophageal outflow tract with associated paintbrush mucosal hemorrhages of the distal esophagus (case 2), as a yellow-tan, protuberant, distal esophageal intraluminal mass (case 5), as a gray, distal esophageal mucosal thickening (cases 7, 11), or as an inconspicuous thickening of the junction of the esophagus and crop reaching the proventriculus, overlain by a granular or roughened mucosal surface resulting in deviation of the crop to the right and marked diffuse compression atrophy of the right lung (case 8). In one of the cases located in the crop (case 2; Fig. 2), the tumor could be palpated through the skin, where it also produced dark-red to purple discoloration. In a field autopsy case (case 4), the esophagus was grossly dark-blue but histologically normal, and intramural SCC was found in the proventriculus. All carcasses were described as thin or emaciated, with moderate to markedly atrophied pectoral musculature and scant fat deposits.

Histologically, SCCs were characterized by neoplastic cells arranged in anastomosing cords and nests (Fig. 3), frequently reaching deep into the submucosa (Fig. 4, Table 2). Although most neoplasms had keratin pearls (Fig. 5), lack of keratin pearls was noted in 2 cases (cases 9, 11). MC was variable and ranged from 3 mitoses/2.37 mm<sup>2</sup> in case 9, to 46 mitoses/2.37 mm<sup>2</sup> in case 8. In most cases, there was ulceration overlain by a mat of fibrin trapping necrotic debris,



**Figures 1–6.** Alimentary squamous cell carcinoma (SCC) in psittacines. **Figure 1.** A firm, light-yellow oral mass extends to the caudal pharyngeal region effacing and replacing the mid-to-caudal portion of the tongue of case 1, a cockatiel (*Nymphicus hollandicus*). **Figure 2.** A variably tan and hemorrhagic, friable mass fills and expands the crop in case 2, a cockatiel (*N. hollandicus*). **Figure 3.** A SCC comprised of anastomosing cords and nests of neoplastic keratinocytes infiltrates, effaces, and replaces the distal esophageal wall in case 8, a macaw (*Ara severus*). H&E. **Figure 4.** A distal esophageal SCC penetrates deep into the mucosa and effaces the junction with the proventriculus in case 8, a macaw (*A. severus*). H&E. **Figure 5.** Neoplastic keratinocytes surround keratin pearls, along with florid heterophilic infiltrates in the distal esophagus in case 8, a macaw (*A. severus*). H&E. **Figure 6.** A single keratin pearl is surrounded by marked fibrosis and smooth muscle bundles at the periphery of the right lung, which is atrophic, in case 8, a macaw (*A. severus*). The atrophic lung is also overlain by large amounts of exfoliated squamous epithelium, necrotic debris, and degranulated heterophils. H&E.

erythrocytes, and inflammatory cells. In case 8, large amounts of fibrosis surrounding smooth muscle bundles and a single keratin pearl were observed at the periphery of the

atrophic lung (Fig. 6). Although no metastases were observed in any case, neoplastic cells were observed within the vasculature of case 11. Additionally, numerous, up to 5- $\mu$ m diameter,

**Table 2.** Major histopathologic findings of alimentary squamous cell carcinomas (SCCs) in psittacines submitted for autopsy or biopsy examination.

Case*	Species	SCC location	Neoplastic cell arrangement	Keratin pearls	Fibroplasia or fibrosis	Necrosis or ulceration	MC (mitoses/2.37 mm <sup>2</sup> )
1	Cockatiel	Tongue, oropharynx	Nests	Y	Y	Y	9
2	Cockatiel	Crop	Nests and anastomosing cords	Y	N	Y	21
3	Cockatiel	Pharyngeal, perilaryngeal	Nests and cords	Y	Y	Y	17
4	Amazon	Proventriculus	Cords	Y	Y	Y	7
5	Amazon	Crop, esophagus	Anastomosing cords	Y	Y	Y	12
7	Amazon	Crop, esophagus, proventriculus	Nests and anastomosing cords	Y	Y	Y	38
8	Macaw	Crop, esophagus, proventriculus	Nests and anastomosing cords	Y	N	Y	46
9	Macaw	Hard palate	Nests and cords	N	N	Y	3
10	Macaw	Oral cavity, rhinotheca	Nests	Y	N	Y	31
11	Parrot	Crop	Nests and cords	N	N	Y	12
12	Conure	Oropharynx, larynx, sinus	Anastomosing cords	Y	N	Y	6

MC = mitotic count; N = no; Y = yes.

\* Case 6 excluded from the table; slides were not available for re-examination.

thin-walled blastospores and blastoconidia arranged in short chains (pseudohyphae) and individual yeast forms were observed in case 8 by PAS stain, and were interpreted as *Candida* sp. as documented previously.<sup>26</sup> Despite the known association of proventricular adenocarcinomas with *Macrorhabdus* sp. in budgerigars,<sup>29</sup> no yeast forms compatible with this organism were identified in any case. Mixed bacteria, predominantly represented by coccobacilli and cocci, were observed in all cases, and were admixed with yeast in cases 4 and 10.

Common opportunistic bacteria isolated from neoplastic tissues included *Streptococcus* sp. and *Staphylococcus* sp. (case 2), *Escherichia coli* (cases 8, 9), or mixed flora (cases 5, 8, 9). No fungi were isolated in the 2 cases in which fungal culture was attempted (cases 5, 9).

The cadmium concentration was above expected in the liver and kidney of case 9 (8 and 43.8 ppm, respectively). Concentrations of the other heavy metals were considered adequate in case 9 and the other 2 tested birds (cases 2, 8). Hepatic concentrations of vitamin A were elevated (673 ppm) in case 12.

Avian influenza A virus and virulent Newcastle disease virus PCR was negative in all cases tested (cases 1, 2, 8, 11, and cases 8, 11, respectively). Avian bornavirus immunohistochemistry was negative on both brain and myenteric plexuses in the only case tested (case 8). No parasites or parasite eggs were found in feces via fecal flotation in cases 8 and 11. *Chlamydia* sp. FAT was negative in cases 1 and 2.

## Discussion

Pet birds, especially psittacines, are overrepresented in the literature of avian neoplastic diseases. This is likely a reflection of their popularity as companion animals, their longevity, and the higher likelihood of patient submission for treatment compared to non-psittacine companion birds (e.g.,

finches). Avian alimentary SCCs are considered uncommon neoplasms in general; most reports refer to poultry.<sup>2,11,40</sup> There are a few, scattered reports of alimentary SCC in psittacines that include an ingluvial SCC in a cockatiel, mandibular SCCs in a green-winged macaw (*Ara chloropterus*), a black-headed caique (*Pionites melanocephalus*) and a Buffon's macaw (*Ara ambiguus*), and esophageal SCCs in 2 Amazon parrots (*Amazona aestiva* and *Amazona fari-nosa*).<sup>10,18,19,35</sup> Retrospective reviews of case submissions to veterinary diagnostic laboratories also revealed a low prevalence of these neoplasms, including cases of oral SCC in an unspecified psittacine and in a red-shouldered macaw (*Diopsittaca nobilis*).<sup>6,10,26</sup>

In our case series, alimentary SCCs occurred in mature psittacines, with a median age of 25 y (average 22.2 y). This is consistent with published reports, in which SCC-affected psittacines had a median age of 22.2 y (average 21.5 y).<sup>6,18</sup> No sex predilection was noticed in our study nor discussed in the literature.

Regurgitation, dysphagia, or observation of an oral mass were common clinical complaints in our study as well as in the literature.<sup>42</sup> In alimentary SCC cases, especially in those affecting the crop, dysphagia can be attributed to either reduction of the ingluvial and/or esophageal lumina because of the physical presence of a mass, or it might have a neurogenic cause if atony of the upper digestive tract occurs as a result of invasion of parasympathetic nerve branches.<sup>18</sup> Dilation of the crop might also prompt consideration of proventricular dilation disease, which is caused by avian bornavirus infection.<sup>12</sup>

In our study, half of the cases arose from multiple sites in the oral cavity, including the choana. Oral SCCs (not including choana) were diagnosed in 25% of cases in a large-scale clinical survey<sup>42</sup>; however, SCCs in other locations within the alimentary tract were not included in that study. The species distribution in the cited large-scale clinical survey<sup>42</sup> and

other studies<sup>18,24,35</sup> matches the findings of our case series, with Amazon parrots and cockatiels significantly overrepresented compared to other psittacines.<sup>10,42</sup>

The crop was the second most commonly affected segment of the alimentary tract. Therefore, it could be hypothesized that an ingluvial SCC might have been the primary focus in the cases with esophageal and/or proventricular involvement. Despite marked local invasiveness, no evidence of metastasis was reported, which is consistent with the documented biological behavior of SCCs in birds.<sup>6,9,26,30</sup> In case 8, it was not clear if the single keratin pearl found in the periphery of the atrophied lung was part of a metastatic focus or simply a point of attachment of the overlying neoplasm. Metastatic alimentary SCC was found in only one report in the literature, which involved a raptor (Montagu's harrier, *Circus pygargus*), with clusters of neoplastic cells that formed micrometastases in the lungs and caused osteolysis in the right tibia and radius.<sup>31</sup> Metastasis of SCCs is more prevalent in other species, such as humans, horses, and dogs, frequently reaching the lungs, liver, spleen, and less commonly the bones.<sup>4,33,39</sup>

As reported elsewhere,<sup>42</sup> necrosis was a prominent histologic feature of alimentary SCCs, most likely related to the rapid turnover of neoplastic keratinocytes. This was the most likely cause of concurrent, opportunistic bacterial or fungal infections in up to 22% of affected birds.

As in other species, conventional diagnostic pathology methods such as cytology and histology are utilized for the diagnosis of SCC in psittacines. Additionally, the use of novel molecular markers such as cyclooxygenase-2 (COX-2), a molecule key in tumor growth, or E-cadherin, a cell adhesion molecule, has been investigated given their prognostic and diagnostic value; the latter seems to be particularly useful to differentiate SCC from mucosal or skin papillomas in small samples.<sup>14</sup> A report concluded that there was a significantly greater proportion of positive cytoplasmic labeling of COX-2 and negative membranous labeling of E-cadherin in SCCs of psittacines compared to papillomas.<sup>14</sup>

The etiology of SCC in psittacines has not been determined, although there is speculation about the role of excessive UV light exposure, chemicals, genetics, diet, reused litter, and infectious agents.<sup>7,25</sup> In some domestic mammalian species, the transition of viral papillomas to SCC is infrequent but well-established.<sup>22,23</sup> However, papillomaviruses do not seem to play a role in the development of mucosal papillomas in psittacine birds.<sup>38</sup> Evidence is mounting toward the association of certain herpesviruses (i.e., *Psittacid alphaherpesvirus 1*) with internal papillomatosis of parrots.<sup>36</sup> However, definitive evidence of the association between viral infection and SCC in psittacines is lacking.

Other predisposing factors for SCC development, such as hypovitaminosis A or chronic wounds, have been discussed,<sup>34</sup> although these are yet to be proven in animals. The bulk of this information is derived from the human literature, which

has investigated the association of epithelial disorders with vitamin A deficiency,<sup>17</sup> and the carcinogenic potential of chronic tissue insult.<sup>14,16</sup> Pet bird diets are usually based on seeds, which are not appropriate sources of vitamin A, and thus may lead to hypovitaminosis A and subsequent squamous metaplasia of the upper alimentary tract. If not corrected, this might progress to malignant transformation.<sup>28,42</sup> Vitamin A was only quantified in case 12, a conure with an oral SCC. Interestingly, squamous metaplasia in glandular tissue of the external ear was detected in this bird (data not shown). Although histologic lesions in this conure were suggestive of hypovitaminosis A, hepatic concentrations (673 ppm) were considered more than adequate when extrapolating normal poultry ranges (60–300 ppm), and according to a study in Australian psittacines in which hepatic vitamin A concentrations were 33–823 ppm.<sup>21</sup> The correlation of hepatic vitamin A levels with true deficiency, and the potential role in SCC development in psittacines, remains to be elucidated.

Above expected hepatic and renal concentrations of cadmium were found in case 9. Cadmium is an environmental pollutant linked to proximal renal tubular epithelial and testicular necrosis in birds and mammals, with ascribed multi-organic carcinogenic effects in humans.<sup>13,20,27</sup> No renal or hepatic lesions were observed in case 9; thus, the clinical significance of this finding to the case or its association with SCC development is undetermined. Detecting cadmium in tissues of adult psittacines is not unusual because it tends to accumulate in the body as the animal ages. A specific cadmium source in case 9 was not identified, but possible cadmium sources for captive birds may include cage material or food dishes (cadmium is found in metal plating and alloys), accidental exposure via small cadmium-nickel batteries, and contaminated feed or drinking water (cadmium can accumulate in plants treated with contaminated fertilizers or sewage sludge).<sup>41</sup>

Multiple therapeutic approaches have been described for avian SCC; however, favorable treatment regimens have not been well-established for most tumors.<sup>32</sup> Treatments include surgery, cryosurgery, electrosurgery, radiation, and intralesional therapy. Inguvotomy was attempted in a cockatiel with ingluvial SCC and, although the bird survived the surgery, complete excision was not possible because neoplastic cells reached the tracheal adventitia, adjacent nerves, and vasculature.<sup>18</sup> Despite the radioresistance of SCCs and low resection success, these neoplasms have a low metastatic rate, and clinical outcome and treatment options might be improved by early detection.<sup>9</sup>

In general, SCCs had poor long-term prognosis and were identified as the cause of death in over 30% of SCC submissions in psittacines according to a retrospective review performed in a veterinary diagnostic laboratory.<sup>9</sup> In our study, type of death was available for 8 cases; alimentary SCC was identified as the cause of death in 5 cases, in 2 additional cases SCC led to euthanasia, and 1 bird died under

anesthesia. Thus, SCC was the most likely contributor to ill-health and death in most of our cases.

There are some limitations to the interpretation of the results in our study, such as the relatively small number of birds included, or the heterogeneity of the ancillary tests requested among the cases. Nevertheless, these limitations do not interfere with one of the main goals of our work, which was to raise further awareness among avian practitioners and pathologists about the varied gross presentations, nonspecific clinical signs, microscopic appearance, species affected, and possible risk factors of SCCs in psittacines. Despite the local aggressive behavior of SCCs, which makes complete resection difficult, an early diagnosis may translate into improved treatment success, hence widening the spectrum of management and therapeutic approaches as well as improving prognostic outcomes.

### Acknowledgments

We thank the pathologists who coordinated the cases included in our study: Drs. Barbara Daft, Hailu Kinde, Rocio Crespo, Janet Moore, H. L. Shivaprasad, and Mark Anderson. We also thank Lucy Gomes for her kind assistance with data mining, and Dr. Robert Poppenga for useful explanations about the heavy metals panel.

### Declaration of conflicting interests

The authors declare no potential conflicts of interest related to the research, authorship, and/or publication of this article.


### Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

### ORCID iDs

Viviana Gonzalez-Astudillo  <https://orcid.org/0000-0003-4208-361X>

Aslı Mete  <https://orcid.org/0000-0002-7612-6713>

Mauricio A. Navarro  <https://orcid.org/0000-0002-7744-8052>

Francisco A. Uzal  <https://orcid.org/0000-0003-0681-1878>

Javier Asin  <https://orcid.org/0000-0002-6178-4801>

### References

1. Abu J, et al. Management of a cutaneous squamous cell carcinoma in an American flamingo (*Phoenicopterus ruber*). *J Avian Med Surg* 2009;23:44–48.
2. Anderson WI, Steinberg H. Primary glossal squamous-cell carcinoma in a Spanish Cochín hen. *Avian Dis* 1989;33:827–828.
3. Beaufrère H, et al. What is your diagnosis? Squamous cell carcinoma of the uropygial gland. *J Avian Med Surg* 2007;21:321–324.
4. Brodey RS, et al. Metastatic bone neoplasms in the dog. *J Am Vet Med Assoc* 1966;148:29–43.
5. Cardona CJ, et al. Squamous-cell carcinoma on the legs of an Araucana chicken. *Avian Dis* 1992;36:474–479.
6. Castro PF, et al. Prevalence of neoplastic diseases in pet birds referred for surgical procedures. *Vet Med Int* 2016;2016:4096801.
7. Fallavena LCB, et al. Presence of avipoxvirus DNA in avian dermal squamous cell carcinoma. *Avian Pathol* 2002;31:241–246.
8. Ferrell ST, et al. Intralesional cisplatin chemotherapy and topical cryotherapy for the control of choanal squamous cell carcinoma in an African penguin (*Spheniscus demersus*). *J Zoo Wildl Med* 2006;37:539–541.
9. Garner M. Overview of tumors. Section II: a retrospective study of case submissions to a specialty diagnostic service. In: Harrison GJ, Lightfoot T, eds. *Clinical Avian Medicine*. 2nd ed. Spix Publishing, 2006:566–572.
10. Halley M, et al. Mandibular squamous cell carcinoma in two psittacines. *J Vet Diagn Invest* 2020;32:344–347.
11. Hatkin J, et al. Inguvial squamous cell carcinoma in a game chicken. *Avian Dis* 2002;46:1070–1075.
12. Hoppes SM, Shivaprasad HL. Update on avian bornavirus and proventricular dilatation disease: diagnostics, pathology, prevalence, and control. *Vet Clin North Am Exot Anim Pract* 2020;23:337–351.
13. Huff J, et al. Cadmium-induced cancers in animals and in humans. *Int J Occup Environ Health* 2007;13:202–212.
14. Jones AL, et al. Avian papilloma and squamous cell carcinoma: a histopathological, immunohistochemical and virological study. *J Comp Pathol* 2020;175:13–23.
15. Klaphake E, et al. Multisite integumentary squamous cell carcinoma in an African grey parrot (*Psittacus erithacus erithacus*). *Vet Rec* 2006;158:593–596.
16. Lin R, et al. Chronic inflammation-associated genomic instability paves the way for human esophageal carcinogenesis. *Oncotarget* 2016;7:24564–24571.
17. Lotan R. Suppression of squamous cell carcinoma growth and differentiation by retinoids. *Cancer Res* 1994;54(7 Suppl):S1987–S1990.
18. Malka S, et al. Inguvial squamous cell carcinoma in a geriatric cockatiel (*Nymphicus hollandicus*). *J Avian Med Surg* 2005;19:234–239.
19. Manucy TK, et al. Squamous cell carcinoma of the mandibular beak in a Buffon's macaw (*Ara ambigua*). *J Avian Med Surg* 1998;12:158–166.
20. Maretová E, et al. Toxic effects of cadmium on testis of birds and mammals: a review. *Anim Reprod Sci* 2015;155:1–10.
21. McDonald D. A review of the nutritional status of wild Australian psittacines. In: *Crocodile Gagudju Kakadu Conf Proc: Psittacine Nutritional Status; Northern Territory*; 2004:73–82. <https://www.aavac.com.au/files/2004-10.pdf>
22. Munday JS, et al. Development of multiple pigmented viral plaques and squamous cell carcinomas in a dog infected by a novel papillomavirus. *Vet Dermatol* 2011;22:104–110.
23. Munday JS, et al. Multiple oral carcinomas associated with a novel papillomavirus in a dog. *J Vet Diagn Invest* 2015;27:221–225.
24. Murtaugh RJ, et al. Squamous cell carcinoma of the esophagus in an Amazon parrot. *J Am Vet Med Assoc* 1986;188:872–873.
25. Nakamura K, et al. Pathology and microbiology of dermal squamous cell carcinoma in young brown chickens reared on reused litter. *Avian Dis* 2010;54:1120–1124.

26. Nemeth NM, et al. A 5-year retrospective review of avian diseases diagnosed at the Department of Pathology, University of Georgia. *J Comp Pathol* 2016;155:105–120.
27. Nicholson JK, Osborn D. Kidney lesions in pelagic seabirds with high tissue levels of cadmium and mercury. *J Zool* 2009;200:99–118.
28. Péron F, Grosset C. The diet of adult psittacids: veterinarian and ethological approaches. *J Anim Physiol Anim Nutr (Berl)* 2014;98:403–416.
29. Powers LV, et al. *Macrorhabdus ornithogaster* infection and spontaneous proventricular adenocarcinoma in budgerigars (*Melopsittacus undulatus*). *Vet Pathol* 2019;56:486–493.
30. Pye GW, et al. Metastatic squamous cell carcinoma in a salmon-crested cockatoo (*Cacatua moluccensis*). *J Avian Med Surg* 1999;13:192–200.
31. Ramis A, et al. Metastatic oral squamous cell carcinoma in a Montagu's harrier (*Circus pigargus*). *J Vet Diagn Invest* 1999;11:191–194.
32. Robat CS, et al. Avian oncology: diseases, diagnostics, and therapeutics. *Vet Clin North Am Exot Anim Pract* 2017;20:57–86.
33. Rocafort Ferrer G, et al. Gastric squamous cell carcinoma in the horse: seven cases (2009–2019). *Equine Vet Educ*. Epub ahead of print 26 November 2020. doi:10.1111/eve.13411.
34. Schmidt RE, Reavill DR. Respiratory system. In: Schmidt RE, et al., eds. *Pathology of Pet and Aviary Birds*. 2nd ed. Wiley, 2015:21–54.
35. Staudenmaier AM, et al. Antemortem diagnosis of esophageal squamous cell carcinoma in a blue-fronted Amazon parrot (*Amazona aestiva*) and a mealy Amazon parrot (*Amazona fari-nosa*). *J Am Vet Med Assoc* 2019;254:1324–1328.
36. Styles DK, et al. Psittacid herpesviruses associated with mucosal papillomas in neotropical parrots. *Virology* 2004;325:24–35.
37. Suedmeyer WK, et al. Attempted photodynamic therapy against patagial squamous cell carcinoma in an African rose-ringed parakeet (*Psittacula krameri*). *J Zoo Wildl Med* 2007;38:597–600.
38. Tachezy R, et al. Avian papillomaviruses: the parrot *Psittacus erithacus* papillomavirus (PePV) genome has a unique organization of the early protein region and is phylogenetically related to the chaffinch papillomavirus. *BMC Microbiol* 2002;2:19.
39. Takagi M, et al. Causes of oral tongue cancer treatment failures. Analysis of autopsy cases. *Cancer* 1992;69:1081–1087.
40. Vazquez S, et al. Squamous cell carcinoma of the oropharynx and esophagus in a Japanese bantam rooster. *Avian Dis* 2003;47:215–217.
41. WHO Int. Nordic Council of Ministers. Cadmium review. Nordic Council, 2003:1–26. [https://www.who.int/ifcs/documents/forums/forum5/nmr\\_cadmium.pdf](https://www.who.int/ifcs/documents/forums/forum5/nmr_cadmium.pdf)
42. Zehnder AM, et al. Clinical features, treatment, and outcomes of cutaneous and oral squamous cell carcinoma in avian species. *J Am Vet Med Assoc* 2018;252:309–315.