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Case Report

Cutaneous hemangiosarcoma in a buff-throated saltator (*Saltator maximus*) with lung metastasis

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Abstract

Hemangiosarcomas are malignant neoplasms arising from endothelial cells of blood vessels. A three-year-old male buff-throated saltator (*Saltator maximus*) was referred to the Veterinary Hospital of the Universidade Federal da Paraíba (HV-UFPB) due to a recurrent tan nodular mass in the pericloacal region. Surgery for excision of the mass was attempted but the bird died during the surgical procedure. The nodule and the carcass were sent for gross and histological evaluation. Histopathology revealed large blood-filled vascular spaces lined by pleomorphic endothelial cells, which were also observed in the lungs. These findings suggested the diagnosis of hemangiosarcoma that was confirmed by immunohistochemistry against factor VIII-related antigen.

Key words: Avian pathology; Neoplasia; Wild Birds; Passeriformes.

Introduction

Hemangiosarcomas are malignant neoplasms arising from endothelial cells (1). These tumors have a high capacity of tissue invasion, and metastases are frequent (7). Grossly, they are characterized by a rounded to irregular soft mass with multiple cavities (12). Bleeding is common due to the disruption of neoplastic vessels. Microscopically, hemangiosarcomas consist of haphazardly arranged irregular defined blood-filled vascular spaces lined by neoplastic plump endothelial cells (1).

There is limited information about hemangiosarcomas in birds and they are more frequently diagnosed inpsittacine birds (6, 8, 10, 13, 19). Avian patients may develop this neoplasm as a single or multiple masses with rapid growth (12). Cockatiels are the birds most frequently diagnosed with this neoplasm, followed by chickens, swans, parrots, lovebirds, parakeets, and few passerine birds (9,10).

This study aims to report a case of cutaneous hemangiosarcoma in a *Saltator maximus* (Statius Muller, 1776), popularly known as buff-throated Saltator.

Case report

A three-year-old male buff-throated saltator (*Saltator maximus*) was referred to the Veterinary Hospital of the Universidade Federal da Paraíba (HV-UFPB) due to a tan pedunculated nodular mass in the pericloacal region (Fig. 1A). A surgical procedure was performed to excise the nodule, but the bird died during surgery. The excised nodule and the carcass were submitted for gross and histologic evaluation at the Veterinary Pathology Laboratory. The bird had had a similar mass in the same anatomic region that was removed a year before.

Grossly, the nodule was 4 x 2.5 x 1 cm, dark red, partially ulcerated and covered with featherless skin. The cut surface presented a brown bloody aspect. Grossly, the lungs were diffusely dark red, and the kidneys were diffusely tan. No significant alterations were observed in other organs.

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Figure 1. A tan, pedunculated, ulcerated mass arises from the pericloacal region (arrowhead).

Tissue samples were fixed in 10%Neutral buffered formalin and processed routinely for histology. Histological sections of neoplasm and lung were submitted to immunohistochemistry (IHC) using polyclonal rabbit anti-human factor VIII-related antigen (FVIII-RA) (Dako North America. Carpinteria, California USA, Ready-to-use) and monoclonal mouse anti-human CD31 (JC70A, Dako North America. Carpinteria, California USA, dilution 1:20) antibodies, employing the universal polymer detection method system (MACH 4 Universal HRP-Polymer, Biocare Medical, Pacheco, California, USA). Romulin AEC chromogen kit was usedas a (Biocare Medical, Pacheco, California, USA). A cutaneous hemangioma from a dog was used for positive and negative controls. Slides were counterstained with Harris haematoxylin.

Histologicevaluation of the excised nodule revealed an unencapsulated poorly demarcated infiltrative neoplasm extending from the superficial to deep dermis and forming a cavernous pattern composed of numerous irregular blood-filled vascular channels lined by plump endothelial cells and also a solid pattern with fewer vascular spaces (Fig.1B). Neoplastic cells had a scarce to moderate amount of eosinophilic cytoplasm with variably distinct cell borders and were supported by a dense fibrous connective tissue stroma.". Nuclei were round to oval with coarsely clumped chromatin and up to 3 evident nucleoli. Anisokaryosis and anisoyitosis were moderate and up to 1 mitosis per 40x high power field (Field area of 0.237 mm2) were observed. There was an extensive area of necrosis amid the neoplasm.

Additionally, large blood-filled vascular spaces were also observed in the lungs. These spaces were lined by pleomorphic cells with indistinct cytoplasm and up to three evident nucleoli. These cells were similar to those present in the primary tumor. Three mitoses per 40x high power field (Field area of 0.237 mm2) were observed. Hemorrhage and congestion were also noted.

Strong positive immunolabeling for FVIII-RA was observed in the cytoplasm of the neoplastic cells lining the vascular spaces of the primary tumor (Fig.1C). On the other hand, the cytoplasm of the neoplastic cells in the solid areas presented a mild positive immunolabeling (Fig.1D). Multifocal immunolabeling for FVIII-RA was also observed in the neoplastic vascular channels in the lungs. Internal positive control and neoplastic cells did not show immunoreactivity for CD31, although the positive control canine tissue exhibited the expected immunolabeling.

Discussion

Vascular neoplasms in avian patients are considered uncommon and the available literature regarding hemangiosarcomas in birds is limited (17). Cockatiels are the avian species with most reports of this neoplasm, but their data is apparently overrepresented due to their popularity as a pet bird (10). The occurrence of hemangiosarcomas has also been reported in other avian species, including

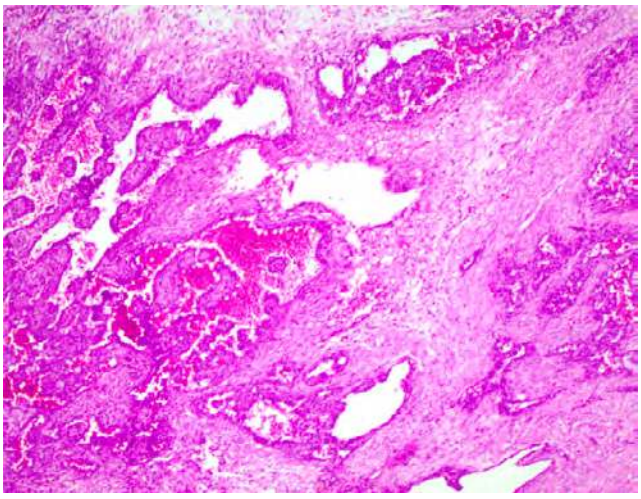

Figure 2. Multiple irregular, blood-filled channels are lined by neoplastic endothelial cells in the deep dermis. Obj. 10x, HE.

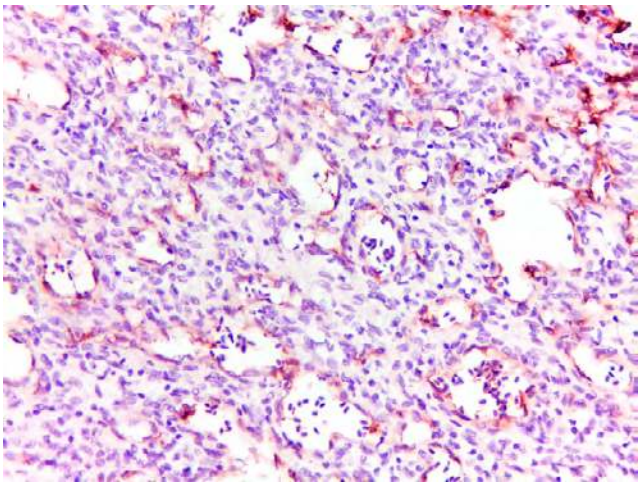

Figure 3. Neoplastic cells have cytoplasmic immunolabeling for FVIII-RA. Obj.20x.

budgerigars (*Melopsittacus undulatus*), lovebirds (*Agapornis* spp.), Amazon parrots (*Amazona* spp.), African grey parrots (*Psittacus erithacus*), pionus parrots (*Pionus* spp.), a Pacific parrolet (*Forpus coelestis*), a golden pheasant (*Chrysolophus pictus*), a swan (*Cygnus* spp.), an ostrich (*Struthio camellus*) and doves (3, 6, 9, 10, 13, 17, 18, 21). Reports of this neoplasm in passerine birds are particularly scarce and restricted to a Java sparrow (*Lonchura oryzivora*), a rufous-bellied thrush (*Turdus rufiventris*), a canary (*Serinus canarius*) and finches (*Fringillidae*) (12, 14, 17).

Hemangiosarcomas in birds are usually invasive, multicentric and metastatic (17). These neoplasms can be coelomic or extracoelomic, and usually, the intracoelomic type is more common, mainly originating from the liver (5, 15, 18) or spleen (15). The primary tumor of the present case was extra-coelomic with metastasis to the lungs. The cutaneous location, as in this case, has been reported as an important site for the manifestation of this tumor in several avian species including *N. hollandicus*, *L. oryzivora*, *F.coelestis*, *Amazona aestiva* and *T. rufiventris* (6, 10, 12, 14, 19).

Although, it is not possible to undoubtedly determine that the cutaneous location of the tumor was the primary site for this neoplasm and that theoretically, a hemangiosarcoma could arise from the vascular endothelium of any body site, primary pulmonary location of intra-coelomic hemangiosarcomas seem to be unlikely in avian patients. Description of Intra-coelomic locations of primary hemangiosarcomas in birds are restricted to the liver (5, 15, 18), spleen (15), ovary (13), pericardium (9) and to the clavicular region (8). In one study, metastases were seen in the kidney, liver and lungs of an amazon parrot, but the authors do not indicate which was the primary site of this neoplasia (5). While there are no reports of primary pulmonary origin of hemangiosarcomas in birds available in the literature, two reports of primary subcutaneous hemangiosarcomas in avian patients have been described (15, 19).

The gross appearance of the nodule was similar to what has been described for hemangiosarcomas in other avian patients. These tumors are usually 1 - 15 cm, dark red to purple nodular soft friable masses with secondary necrosis and ulceration (12, 17). Histologically, the tumor features are also corroborated by other descriptions of hemangiosarcomas in birds (5, 6, 9, 14, 18), which describe the exuberant irregular angiogenesis accompanied by a low mitotic count, as the main microscopic feature of this tumor.

Hypotensive shock due to hemorrhage secondary to tumor rupture is the most frequent cause of death associated with hemangiosarcomas (2). The hemorrhage observed in the lungs of the buff-throated saltator might have contributed to the intraoperative cause of death, causing hypotensive shock or causing the functional impairment of a vital organ.

Similar to the present case, metastasis of cutaneous hemangiosarcomas has been reported in a *F.coelestis* in which the primary tumor developed in the metatarsal pad and spread to liver and kidney (14). Involvement of other organs, including ovary, heart, and carotid artery has also been reported in birds (8, 13, 17).

Differential diagnoses of hemangiosarcomas in birds may include benign masses, such as hematomas and hemangiomas, due to their reddish to dark red gross appearance, and also malignant tumors such as squamous cell carcinomas, fibrosarcomas and melanomas, as they can have a similar reddish to dark red ulcerated gross appearance (10, 17). In contrast to hemangiomas, surgical removal of hemangiosarcomas may not be curative, and local regrowth within days to months is common (17).

A definitive diagnosis of hemangiosarcoma relies on histology and IHC for FVIII-RA or CD31. However, some antibodies may have low reactivity in avian tissues or lack an optimized protocol for IHC in birds (14), which could explain the lack of immunolabeling for CD31 in the present case. Discrepancy for FVIII-RA immunolabeling, especially between cavernous and solid patterns, have also been described in the literature(16, 22), which might explain the weak immunolabeling for FVIII-RA in the solid areas of the present tumor. Several etiologies have been speculated as a putative cause for hemangiosarcomas in birds. Chronic inflammation induced by trauma has been implicated as an important triggering factor for this neoplasm, once the oxidative damage to DNA and induction of angiogenesis, provide an ideal environment for oncogenesis (10). In poultry, retroviruses have been associated with the development of vascular tumors (11, 20), however, there are no studies that indicate that a similar association may occur in wild and exotic birds, and the one study that aimed to search for retroviral particles in spontaneous tumors of the parakeet (4) was not able to find any detectable viral particles in these tumors.

This neoplasm should be considered as a differential diagnosis for cutaneous nodular masses in passerine birds, and its metastatic potential to vital organs should be taken into consideration as can culminate in a life-threatening condition for avian patients.

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