Hemangiosarcoma with Widespread Metastasis that Originated on the Metatarsal Pad of a Java Sparrow (Padda oryzivora)

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Abstract. A five-year-old male Java sparrow (Padda oryzivora) was examined because of the appearance of a purple spot approximately 1 mm in diameter on the right metatarsal pad. Seven months later, the spot spread to the entire right leg, and the bird died. At necropsy, multiple neoplastic masses on the right leg reached up to the pelvic cavity. There was one similar mass on the right kidney and multiple red spots on the liver. Histopathological examination revealed that neoplastic cells proliferated solidly or formed abundant irregular blood vessels. Watanabe silver staining revealed that neoplastic cells were surrounded by argentophil fibers. Immunohistochemically, the neoplastic cells were positive for anti-human von Willebrand factor antibodies. This is the first report of hemangiosarcoma in a finch.

Key Words: finch, hemangiosarcoma, Java sparrow, metastasis.

Hemangiosarcoma is a malignant tumor that develops from vascular endothelial mother cells. The tumor, which is characterized by abundant angiogenesis, readily undergoes metastasis and has a high degree of malignancy [6]. Although hemangiosarcoma has been reported in poultry [3], it has only been reported in nine cases of pet psittaciiform birds [4, 7, 9–11, 13] and has not yet been found in finches. Here, we report the discovery of hemangiosarcoma with widespread metastasis in a Java sparrow (Padda oryzivora).

The bird was a 5-year-old male brought to the clinic due to the formation of a purple spot 1 mm in diameter on the right metatarsal pad at the base of the first digit (Fig. 1, inset). According to the bird’s owner, the skin of the entire right leg had begun to periodically turn dark red a few months previously. X-ray examination revealed no fracture or other bone lesion and showed no other abnormal organs. The 16th day after the initial examination, the entire right leg swelled, and hemorrhaging was observed across a wide area of the skin surrounding the heel. The first purple spot spread across the plantar region, after which purple spots approximately 1 mm in diameter appeared on the digits. The bird was not in pain; it was healthy with a good appetite, and there was no dysfunction of the right leg. On the 60th day after the initial examination, the bird began to self-mutilate the affected area, and the swelling was diminished by bleeding. On the 90th day, the affected region began to disintegrate. The pattern of swelling, bleeding and disintegration repeated itself, and after six months, dark red neoplastic masses of various sizes occurred throughout the right leg. Also, it could be seen through the skin that the liver was swollen and contained scattered dark red spot. Seven months after the initial examination, the bird died, and a necropsy was performed. The various tissues with neoplastic mass were fixed in 10% phosphate-buffered formalin for histological and immunohistochemical analysis. Calcium salts were removed from tissue including bone using K-CX (Falma Co., Ltd., Tokyo, Japan). Tissue was embedded in paraffin and sectioned at approximately 4 µm for hematoxylin-eosin (HE), silver (Watanabe method) and immunohistochemical staining. Immunohistochemistry was performed using primary mouse monoclonal antibodies to human von Willebrand factor (polyclonal rabbit; DakoCytomation Denmark A/S). Secondary antibody reaction was performed using a peroxidase-conjugated Histofine Simple Stain MAX PO kit (Nichirei, Tokyo, Japan). Reaction products were visualized using 3′3-diaminobenzidine. The slides were counterstained with Mayer’s hematoxylin.

On gross examination, the tips of the digits on the right foot were necrotic (Fig. 1). There was extensive subcutaneous hemorrhaging in the tarsus, and multiple dark red neoplastic masses were found in the right leg: a similar mass found in the right kidney. The right leg masses ranged in size from 1 to 5 mm in diameter. Neoplastic masses of the medial thigh reached up to the pelvic cavity through the right ischiadic foramen and puboischicadic notch and were in contact with the kidney (Fig. 2, inset A). An approximately 10 × 8 mm renal mass on the anterior lobe of the right kidney displaced the right-testis (Fig. 2, inset B). The liver was swollen and brittle and diffusely scattered with dark red spots 1–2 mm in diameter (Fig. 3). All of the parenchymal organs had the appearance of advanced anemia.
Fig. 1. Seven months after the initial examination, the bird died. Tips of the digits were necrotic, and irregular dark red neoplastic masses were observed (arrows). Inset: Initial examination; the first purple spot was observed on the metatarsal pad (arrow).

Fig. 2. Neoplastic masses (arrows) of the medial thigh reached up to the pelvic cavity through the right ischiadic foramen (white arrow) and puboischiadic notch and were in contact with the kidney. Inset: The renal mass is the portion surrounded by the white dotted line. (A) Dorsal kidney. The mass was in contact with the right ischiadic foramen. (B) Ventral kidney. Normal left-testis (white arrow) and displaced right-testis (arrow).

Fig. 3. The liver was swollen, brittle and diffusely scattered with dark red spots.

Fig. 4. In the area with abundant blood vessels, neoplastic blood vessels were irregular in shape. Spindle-shaped to round tumor cells proliferated around the blood vessels. HE. Bar=100 μm.

Fig. 5. In the solid area, spindle-shaped to round neoplastic cells either proliferated in a sheet or had a cobblestone appearance, with clefs observed between neoplastic cells. HE. Bar=50 μm.

Fig. 6. Argentophil fibers appeared to surround multiple neoplastic cells in the area surrounding the neoplastic blood vessels and in the solid growth area. Watanabe silver stain. Bar=100 μm.

Fig. 7. Neoplastic cells were positive for anti-human VWF antibodies. Bar=25 μm.
In addition, moderate pericardial effusion was observed. Histopathologically, the dark red masses on the right leg, the renal mass and the dark red spots on the liver all exhibited identical histology. The neoplastic mass was comprised of two areas, an area with abundant blood vessels and a solid area with few blood vessels. The neoplastic blood vessels were irregular in shape, and spindle-shaped to round cells proliferated around the blood vessels (Fig. 4). In the solid area, spindle-shaped to round cells either proliferated in a sheet or had a cobblestone appearance, with clefts observed between neoplastic cells (Fig. 5). In both areas, neoplastic cells had indistinct cytoplasmic boundaries, exhibited anisokaryosis and had weakly acidophilic cytoplasm, and highly atypical cells were scattered in each area. Neoplastic cells had infiltrated the bone marrow of the right tarsometatarsus. In the liver, the neoplastic cells formed large blood vessels and showed intraparenchymal infiltration and proliferation, compressing liver tissue. The renal mass was made up of an area of solid proliferation that was solitary and well circumscribed within the renal parenchyma. Mitotic figures were rare. Watanabe silver staining revealed that neoplastic cells in the area surrounding the neoplastic blood vessels and in the solid growth area were surrounded by argentophil fibers (Fig. 6). In addition, not only the normal vascular endothelium but also the lumen-forming neoplastic cells and solid proliferation area were positive for anti-human VWF antibodies (Fig. 7).

The diagnosis of hemangiosarcoma was confirmed by the results of gross examination, histopathology and immunohistochemistry. Von Willebrand factor (VWF) is widely used to diagnose hemangiosarcoma and is regarded as a useful vascular endothelial marker [5]. However, previous studies have shown that anti-human VWF antibodies used in humans have low reactivity with avian tissue [7]. The diagnosis of the present study is considered conclusive because the cells that comprised the areas of angiogenesis and solid proliferation, as well as an internal positive control (normal endothelial cells), were all positive. The only reported cases of hemangiosarcoma in pet birds have been five cases in budgerigars [4, 10], one case in a cockatiel [13] and three cases in Amazon parrots [7, 9, 11]. No cases have been reported in finches, making the present case the first report. Also, while exposure to vinyl chloride or AsO₂-containing insecticides and long-term administration of androgenic anabolic steroid and estrogen are all known to induce hemangiosarcoma in humans [2], none of these apply to the present case, and the cause of onset remains unclear. Hemangiosarcoma is highly infiltrative with poor prognosis, and hemorrhage due to rupture of the tumor is believed to be a frequent cause of death in mammals with this condition [5, 6]. Sudden hemorrhaging from the tumor was not observed in the present case, but continual hemorrhage from the tumor on the right leg and anemia were found toward the end of life. As there was retention of pericardial effusion, we surmise that there was a decrease in plasma osmolality at the end of life and that death was due to hypovolemic shock.

REFERENCES

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**Comments**

[Q1] Medline reports the issue should be “1” not “Apr” in reference 1 “Carter, Proctor, Smith, 1983”.


[Q3] Medline reports the volume should be “53” not “A53” in reference 13 “Sledge, Radi, Miller, Lynn, 2006”.