Opis przypadku *Case report*

Successive therapy of squamous cell carcinoma in African grey parrot

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Summary

A 25-year-old male African grey parrot (Psittacus erithacus erithacus) with a non healing wound on the plantar surface of the right tarsometatarsus has been presented. Initial treatment with enrofloxacin and wound management was unsuccessful. Bacteriology was negative. Histopathological examination of collected samples indicated squamous cell carcinoma.

Therapy was started with electrosurgery of the damaged tissue. Adjacent tissues were injected with carboplatin/sesame oil emulsion. Intravenous chemotherapy with carboplatin (5 mg/kg b.w.) was administered after 2 and then 3 weeks. Since carcinoma was diagnosed, Cats claw extract (Uncaria tomentosa) has been also administered. Despite of problems with severe inflammation for the first few weeks after surgery and necrosis of one toe, damages have been completely healed, and the patient's mental and body conditions were significantly improved.

Keywords: parrots, squamous cell carcinoma, chemotherapy

Epithelial tumors in birds originate in the surface epithelium, follicular epithelium or the uropygial glands. Squamous cell carcinomas (SCC) are often ulcerated and hemorrhagic, as well as infiltrative. SCC was diagnosed in pet birds (4, 8, 11, 13, 20, 21) as well as in wild birds (12). This type of neoplasia may occur anywhere on the body, being most prevalent at mucocutaneous junctions of the head on the distal wing and on the phalanges (4, 12, 13, 20, 21). Metastasis is not common, but occurs, particularly in chronic cases (16). Squamous cell carcinoma frequently appears grossly as a delayed or non-healing cutaneous infection, and diagnosis is therefore often delayed (11).

Traditionally, the most common approach to the treatment of neoplasia in birds has been surgical excision or limb amputation (6, 9, 12). Radiation therapy may also be used with moderate sensitivity in a palliative setting to relieve discomfort or obstruction with or without adjunct surgery (14). Photodynamic therapy can also be used in avian SCC treatment to reduce tumor burden (19). Intralesional therapy has also been explored with carboplatin and cisplatin and has yielded varying results (5, 6, 8, 9). Carboplatin is a second--generation, platinum containing chemotherapeutic agent that is less nephrotoxic and emetogenic than cisplatin in dogs and cats. Carboplatin has been used successfully for the treatment of a bile duct carcinoma in a yellow-naped Amazon parrot (*Amazona ochrocephala*) and pancreatic duct adenocarcinoma in a green-winged macaw (*Ara chloroptera*) (17).

Case history

A twenty-five-year-old African grey parrot (*Psittacus erithacus erithacus*) was presented to the avian disease ambulatory Faculty of Veterinary Medicine, Warsaw University of Life Sciences, because of a non-healing wound on the plantar surface of right tarsometatarsus (Fig. 1). The wound was covered by caseous exudates, present also under undamaged skin of the heel (Fig. 2). For the next 4 weeks the case was treated with enrofloxacin 10 mg/kg/12 h Enroxil (KRKA), meloxicam 0.2 mg/kg/24 h Metacam (Boehriniger) and dietary supplementation directions have been made. Twice a week the wound was flushed with antibiotic solution (Linco-spectin, Medivet) and treated with Pana-veyxal (Veyx-Pharma) ointment, but without improvement. The left limb was also treated and bandaged because of early stages of bumble foot.

Almost every time extensive bleeding occurred during wound cleaning. On the day first and a month later swabs from the wound and feces for bacteriology were taken. Slide stained with Ziehl-Neelsen method was also made. Bacteriology and Z-N staining were negative.

Fig. 1. Non healing ulceration connected with squamous cell carcinoma on the plantar surface of right tarsometatarsus

Fig. 2. Caseous exudate in the heel and upper tarsometatarsus region, emerged after skin resection

Histopathologic examination of the tissues sampled from indolent wounds revealed undifferentiated *carcinoma planoepitheliale* with purulent inflammation and extensive necrotic areas (Fig. 3).

Tumor therapy was started with electrosurgery of the damaged tissue. Adjacent places were injected with carboplatin (Carboplatin 10 mg/ml, Pfizer) as a 3.3 mg/mL water/sesame oil emulsion. The dose of carboplatin was 5 mg/kg b.w. (5, 6). After surgery maloxicam 0.2 mg/kg was administered for 7 days, then calecoxib (Celebrex, Searle) at a dose of 10 mg/kg for 4 weeks. Intravenous chemotherapy with carboplatin (5 mg/kg in 20 ml 5% glucose solution slowly to the brachial vein) was administered after 2 then 3 weeks. Since the day of surgery the owner has administered her parrot 1/3 of 400 mg capsule of Cats claw extract (*Uncaria tomentosa*).

Surgery and chemotherapy procedures were made under isoflurane (2, 5%) anesthesia.

Two weeks after surgery the limb was more painful and swollen, the first and distal parts of the third finger were necrotized. Loss of body weight and weakening was observed. The wound was treated with Povidone iodine (Polfa Kutno) and 7 days of antibiotic therapy was administered. After the following month all damages have been completely healed (Fig. 4), mental and body conditions were significantly improved. During 12-months of clinical observation there was no evidence any health problems in the treated parrot.

Before and during the course of therapy the hematology and blood biochemistry were examined. Blood samples were collected from the right jugular vein. Total red (RBC) and white blood cell counts (WBC) were performed with the Natt-Herrick's solution and Neubauer hemocytometer. The hematocrit value (PCV) was determined using microhematocrit capillary tubes and centrigfuge. Hemoglobin concentration was estimated by the cyanomethemoglobin method and red cell indices (MCV, MCH and MCHC) were calculated by using the standard formulas. The leucogram was performed on blood smears stained with the May-Grűnwald-Giemsa method (3). The values obtained are

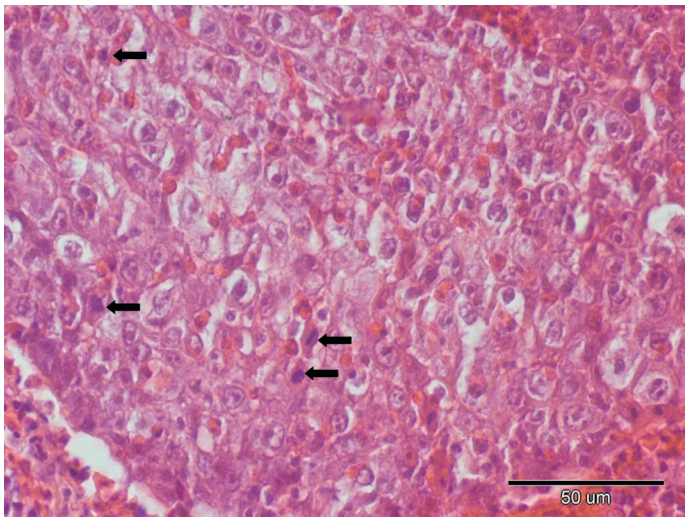

Fig. 3. Poorly differentiated squamous cell carcinoma. Arrows show 4 mitotic figures in this field. Original magnification 40×, H-E staining

Fig. 4. The leg two months after surgery

Tab. 1. Blood haematology and chemistry

Determination	First visit 5 weeks before surgery	Day of the surgery (carboplatin locally)	2 weeks after surgery (carboplatin i.v.)	5 weeks after surgery (carboplatin i.v.)	8 weeks after surgery	Reference	
						Harrison & Lightfoot (7)	Samour (18)
RBC × 10^{12}/l	–	2.48	2.98	2.10	3.84	2.4-3.9	2.4-4.5
Ht [%]	–	27	20.5	23.5	35.5	40-48	43-55
Hb [g/dl]	–	5.46	5.42	7.9	13.25	–	14.2-17
MCV [µm^3]	–	108.9	68.8	111.9	92.4	–	137-135
MCH [pg]	–	22.0	18.2	37.6	34.5	–	41.9-52.8
MCHC [g/dl]	–	20.2	26.4	33.6	37.3	–	28.9-34
WBC × 10^9/l	–	11.2	28.38	19.1	8.5	5-11	5-11
Lymphs [%]	–	63	19	48	50	25-45	20-50
Hets [%]	–	31	80	44	45	55-75	45-75
Baso [%]	–	2	0	3	2	0-1	0-5
Monocythes [%]	–	1	0	4	2	0-3	0-3
Eosinophiles [%]	–	0	1	1	1	0-2	0-2
Amylase [U/L]	–	273.4	–	–	414	210-530	211-519
AST [U/L]	90	76.4	–	–	87.7	100-365	28-200
CPK [U/L]	–	358.0	–	–	373.5	165-412	71-408
LDH [U/L]	–	359.1	–	–	399.5	145-465	105-420
Total protein [g/dL]	3.5	2.9	–	–	4.0	3-4.6	3.2-4.4
Glucose [mg/dL]	–	260.1	–	–	258.2	190-350	205.2-289.8
Creatinine [mg/dL]	0.6	–	–	–	–	0.1-0.4	0.1-0.4
Uric acid [mg/dL]	6.1	1.6	–	–	2.7	4.5-9.5	3.1-7
Calcium [mg/dL]	7.0	7.2	–	–	8.5	8.5-13	7-9.5
Potassium [mmol/L]	–	3.32	–	–	2.2	2.9-4.6	2.5-3.9
Sodium [mmol/L]	–	160.72	–	–	149.6	157-165	154-164
Phosphorus [mg/dL]	2.8	4.6	–	–	1.1	3.2- 5.4	1-5.2

presented in Table 1. Red blood cell parameters varied significantly during therapy because of anemia. WBC parameters were the highest 2 and 5 weeks after surgery, possibly because of inflammation. After surgery (8 weeks) hematology and plasma biochemistry values appeared to be in normal range for this avian species (18).

Discussion

The leg's skin ulcerations in parrots may be result of many factors: e.g. nutritional deficiencies, improper perches, immune mediated disorders, trauma, as well as behavioral problems, bacterial, fungal or viral infections (2). Abnormal pink coloration of the contour feathers has been linked to circovirus or a dietary imbalance (7). In the presented case psittacine circovirus PCR test (22) was negative from the feathers and blood samples. Nutritional problems may be also confirmed by low level of blood plasma calcium. But African grey parrots are especially prone to calcium level imbalance (10). Chronic malnutrition could be a cause of immunosuppresion, which is a risk factor for cancer.

Avian carcinoma can cause mainly ulcerative, but sometimes also nodular lesions. Fibrinous or caseous exudates along the ulceration were observed also in the other described cases of squamous cell carcinoma in birds (16).

During primary antibacterial therapy this exudate renewed a few days after wound cleaning. After electrosurgery the wound was covered only by a dry crust.

Purified sesame oil in the formulation significantly reduced systemic exposure to carboplatin and drug leakage from the sites of injection. Probably edema and necrotic changes of digits together with marked leucocythosis observed two weeks after surgery were caused by carboplatin or sesame oil irritation (the used sesame oil was good quality food oil centrifuged 14 000/min for 10 min [with no sediment], filtrated with Millex® -HV 0.45 µm filter unit (Millipore) and warmed 30 min at 90°C) or mechanical compression of the injected suspension on blood vessels or their damage during surgery.

Significant anemia noted 5 weeks after surgery was an effect of carboplatin treatment, but also of blood

loss during cleaning of the wound. It is questionable how significant in the therapy was using *Uncaria tomentosa* extract, immunomodulatory, anticancer and anti-inflammatory herbal remedy (15). Belthegi et al (1) revealed that *Uncaria tomentosa* administration in rabbits has generated a significant increase of the lymphocyte count, and therefore of the total circulant leukocyte count, aspects that indicate a stimulating effect upon the adaptive immune response (1); our case in respect to lymphocytes confirms this observations. Results of hematology and plasma biochemistry confirmed that hematological and biochemical parameters are useful indicators in monitoring clinical health status of during chemotherapy.

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