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Clinical Report

Uropygial Gland Keratoacanthoma in a Saker Falcon (*Falco cherrug*) Associated With Herpesvirus Infection: Clinical and Pathological Findings

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Abstract: A 24-year-old female saker falcon (*Falco cherrug*) was presented for a hyperkeratotic lesion associated with the uropygial gland. Owing to perceived anesthetic risks, a conservative medical approach was initially chosen over surgical excision. The treatment involved local debridement and supportive care, which provided temporary improvement. However, the lesion recurred multiple times, leading to the decision to perform complete surgical excision of the uropygial gland. The falcon underwent cardiopulmonary arrest during the procedure and was unresponsive to resuscitation. Histological analysis identified a compact cystic mass characterized by atypical proliferation of the keratin and squamous cell layers, consistent with an infiltrating keratoacanthoma of the uropygial gland. Additional findings included necrotizing hepatitis, focal splenic necrotic lesions and white pulp depletion, pyogranulomatous nephritis, pulmonary edema, and infiltrative chronic-active enteritis. Amphophilic intranuclear inclusion bodies were observed in the basal layer of the uropygial mass and in hepatocytes. Immunohistochemistry confirmed the presence of avian alpha-herpesvirus antigen in liver, kidney, and uropygial gland. To the authors' knowledge, this is the first documented case of uropygial keratoacanthoma in a bird of prey.

Key words: saker falcon, *Falco cherrug*, avian, keratoacanthoma, uropygial gland, alpha-herpesvirus

CLINICAL REPORT

A 24-year-old, 1.001-kg female saker falcon (*Falco cherrug*) housed in an outdoor aviary at Zoomarine Algarve (Faro, Portugal) was presented with a noticeable swelling at the base of its tail. The falcon's diet was composed of quail, rats, and day-old chicks. As part of the zoological collection, this bird was included in a routine preventative medicine program. The falcon's medical history included bilateral nuclear sclerosis diagnosed at 18-years-old and dilated cardiomyopathy diagnosed at 21-years-old. The falcon was routinely monitored (clinical signs, physical examination, electrocardiograms, echocardiography) and remained stable on a treatment regimen of benazepril (0.5 mg/kg PO q24h; Fortekor, Elanco GmbH, Cuxhaven, Germany) and pimobendan (0.25 mg/kg PO q12h; Cardisure, Eurovet Animal Health BV, Bladel, the Netherlands).

Following the initial presentation (day 0), a clinical examination was conducted under general anesthesia with isoflurane (2–5% in a 2-L/min flow of oxygen; IsoFlo, Zoetis Spain, S.L., Madrid, Spain). Anesthetic monitoring was based on evaluation of the bird's respiratory pattern (rate, depth, and character of breathing) together with cardiovascular assessment through cardiac auscultation and Doppler equipment (Shenzhen Bestman Instrument Co., Shenzhen, China) placed over the ulnar artery to evaluate heart rate stability, rhythm, sound quality, and contraction strength. All subsequent follow-up examinations used this same anesthetic protocol. The examination was unremarkable apart from a dull appearance to the feathers and a hyperkeratotic lesion associated with the uropygial gland, with layered, multiple yellow firm masses with fistulous tracts. There was

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Figure 1. Keratoacanthoma of the uropygial gland of a 24-year-old saker falcon (*Falco cherrug*) after debridement (insert, surgically removed keratinous material).

no evidence of skin proliferation in other areas. Because of the anesthetic risks associated with complete surgical excision of the uropygial gland, a conservative medical approach was initially chosen. Local tissue debridement was performed, and the gland was flushed with F10 SC (F10 Products Limited, Loughborough, United Kingdom) diluted 1:250 with NaCl 0.9% (B. Braun, Melsungen, Germany) (Fig 1). The patient was initially treated with systemic antibiotics (amoxicillin trihydrate with clavulanic acid, 125 mg/kg PO q12h × 15 days; Kesium, Ceva Santé Animale, Libourne, France) and anti-inflammatory medication (meloxicam, 1mg/kg PO q24h × 10 days; Meloxidyl, Ceva Santé Animale), along with flushing of the uropygial gland with F10 SC diluted 1:250 with saline (q12–24h × 120 days) without physical restraint. The debrided mass was submitted for histopathologic analysis, which confirmed keratin proliferation (Laboratory DNATech, Lisbon, Portugal).

A follow-up examination on day 7 showed significant improvement over the initial findings, and by day 84 there were no signs of impaction or proliferation associated with the uropygial gland. However, on day 111, a recheck examination confirmed partial recurrence of gland impaction, with no obvious hyperkeratotic layers. Digital pressure was applied to the gland, expressing a thick, pasty, yellowish secretion. A sample was collected for cytological examination, but it was unremarkable. A bacterial culture was positive for *Staphylococcus* sp (Faculdade de Medicina Veterinária – Laboratório de Microbiologia e Imunologia, Lisbon, Portugal), with no detected antibiotic resistance, and an in-house fungal culture was negative. Blood was collected from the right jugular vein for an in-house complete blood count and a biochemistry panel, using a Vetscan chemistry analyzer and Avian/Reptilian Profile Plus (Abaxis Europe GmbH, Griesheim, Germany).

The total erythrocyte and leukocyte counts were performed manually. Briefly, 5 µL of a blood-filled pipette was inserted into a Natt-Herricks-TIC 1:200 stain solution vial (Bioanalytic GmbH, Umkirch, Germany), and counting was performed with a hemacytomer.[1] Evaluation of blood smears was performed after Diff-Quik staining (MAIM S.L., Barcelona, Spain). Hemoglobin concentrations were obtained through a hemoglobin analyzer (HemoCue, Ängelholm, Sweden), and hematocrit values were obtained after centrifugation of microhematocrit tubes (12,000 rpm × 5 minutes; Centurion Scientific Ltd - Pro-Vet, Sussex, United Kingdom). Blood results were within normal limits at the initial examination and subsequent analyses throughout the clinical case. After these diagnostic results, the patient was treated with marbofloxacin (5 mg/kg PO q24h × 7 days; Marbocyl, Vétoquinol, Lure, France) and meloxicam (1 mg/kg PO q24h × 5 days), along with flushing the uropygial gland with diluted F10 SC as previously described.

On day 150, a noticeable reduction in preening behavior was reported, along with evident orthopedic discomfort, suggesting an aggravation of the previously diagnosed osteoarthritis. Gabapentin (10 mg/kg PO q24h; Gabapentina ratiopharm, Merckle GmbH, Blaubeuren, Germany) was prescribed as well as silymarin (140 mg PO q24h; Legalon, Madaus GmbH, Cologne, Germany). Recheck examinations at this time showed a slight impaction of the uropygial gland with no fistula or indication of local inflammation.

On day 320, clinical reevaluation showed ulceration at 2 distinct sites on the right lobe of the uropygial gland, which appeared severely deformed and impacted. In addition to the previously described general anesthetic protocol, local anesthesia was provided by subcutaneous injection of 2 mL of lidocaine (Lidor 2%, VetViva Richter, Wels, Austria) around the periphery of the gland. Partial surgical excision (approximately 60%) of the right side of the gland was performed. A scalpel blade was used for the initial incision of the caudal

aspect of the right lobe, followed by blunt dissection of the glandular tissue. The skin was closed using simple interrupted sutures (Monosyn 3-0, B. Braun), maintaining a 5-mm caudal opening for flushing with the diluted F10 SC solution. Histopathological analysis of the resected tissue confirmed a cystic mass comprised of stratified keratin arranged in concentric scales that merged into an amorphous material in the central area of the cyst (Fig 2A).

In the weeks after surgery, the falcon appeared more comfortable, exhibiting improved preening behavior and increased activity. A follow-up examination on day 366 did not identify any signs of impaction; however, fluid secretion was observed on the left side of the gland. By day 423, a severe impaction recurred on the left side of the uropygial gland, prompting the veterinary team to opt for complete surgical excision. The general inhalant and local anesthesia protocols and planned surgical techniques were like those performed on the right side of the gland on day 320; however, the plan was to completely excise the glandular tissue. Immediately after complete excision of the uropygial gland and skin closure, the falcon developed apnea, which was rapidly followed by cardiac arrest. The bird was unresponsive to doxapram (20 mg/kg; Dopram, Eumedica SA, Brussels, Belgium) and epinephrine (1 mg/kg; Adrenalina, B. Braun, Queluz de Baixo, Portugal) therapies delivered via the jugular vein.

A complete postmortem examination was performed. There were multifocal areas of congestion on the liver surface and within the parenchyma. Cardiac examination confirmed the in vivo echocardiography findings showing enlargement of both ventricles. However, intracardiac measurements remained stable since the initial diagnosis and initiation of the treatment. Histopathological examination was carried out according to standard protocols.[2] The surgically excised uropygial gland had atypical proliferation of keratin and squamous cell layers, consistent with an infiltrating keratoacanthoma (KA) of the uropygial gland (Fig 2B). The tumor was characterized by a central keratin-filled cavity surrounded by symmetrical epidermal horns or spurs. Intralesional cell proliferation predominantly consisted of well-differentiated epithelial cells. Mitoses, primarily typical, were mainly observed in the basal layer of the epidermis (Fig 2C). The tumor was frequently associated with vascular stroma, with lymphocytic, histiocytic, heterophilic, and eosinophilic infiltration. A well-defined interface between the tumor and the underlying subcutaneous tissue was generally present (Fig 2B). Squamous cells with abundant central cytoplasm and no significant cellular atypia were also observed. Additionally, amphophilic endonuclear inclusions, also observed in the liver, were noted at the nuclear level of the scattered neoplastic cells of the basal layer of the uropygial tumor (Fig 2C).

A systemic, generalized congestive-hemorrhagic state with multiple pathological changes was observed (Figs 2C). The liver exhibited focal and severe necrotizing hepatitis, characterized by intense mononuclear cell infiltration in the perivenous areas and foci of karyorrhectic phenomena within the hepatic parenchyma (Fig 2D). The liver parenchyma showed vacuolar-hydropic degeneration and a diffusely swollen appearance of the hepatocytes. A widespread pattern of nuclear aberrations was observed in liver cells, with scattered eosinophilic-amphophilic endonuclear inclusions, identical to those observed in the KA. In these nuclei, a reinforcement of the chromatin was evident near the nuclear membrane, accentuating the amphophilic aspect of the nucleoplasm.

The kidneys exhibited multiple urate deposits and severe lesions consistent with interstitial nephritis, characterized by foci of interstitial lymphomonocytic infiltrates. In the gastrointestinal tract, pyogranulomatous-infiltrative enteritis was observed, affecting most of the intestinal loops. Pulmonary changes included interstitial and alveolar edema. The spleen displayed focal necrotic lesions, severe depletion of the white pulp, and small intrasplenic granulomas with a necrotic center surrounded by a giant cell (Langhans-type) reaction.

The presence of intranuclear eosinophilic-amphophilic inclusion bodies in both hepatocytes and the KA was suggestive of a herpesvirus infection, prompting a immunohistochemistry assay (IHC) to be performed. The following 2 different anti-avian herpesvirus antibodies were used: anti-infectious laryngotracheitis virus (ILTV) and anti-Marek's disease virus. Antigen screening was performed on 3-μm-thick paraffin-embedded sections of the liver, kidney, and uropygial gland following standard protocols.[2] The IHC was positive for ILTV antigen in the uropygial gland (Fig 2B), liver (Fig 2E), and kidney (Fig 2F). Conversely, anti-Marek's disease virus antigen was negative in all tested samples.

DISCUSSION

This report outlines the medical and surgical management of a recurrent keratin proliferation and impaction of the uropygial gland in a geriatric female saker falcon. The uropygial gland is a bilobed gland that produces a lipoid sebaceous secretion, which is spread on the plumage during preening.[3–5] Our understanding of the roles secretions play in birds' plumage is still in its infancy.[6,7] Pathology of the uropygial gland may lead to poor feather quality, as observed in this case, as well as difficulties

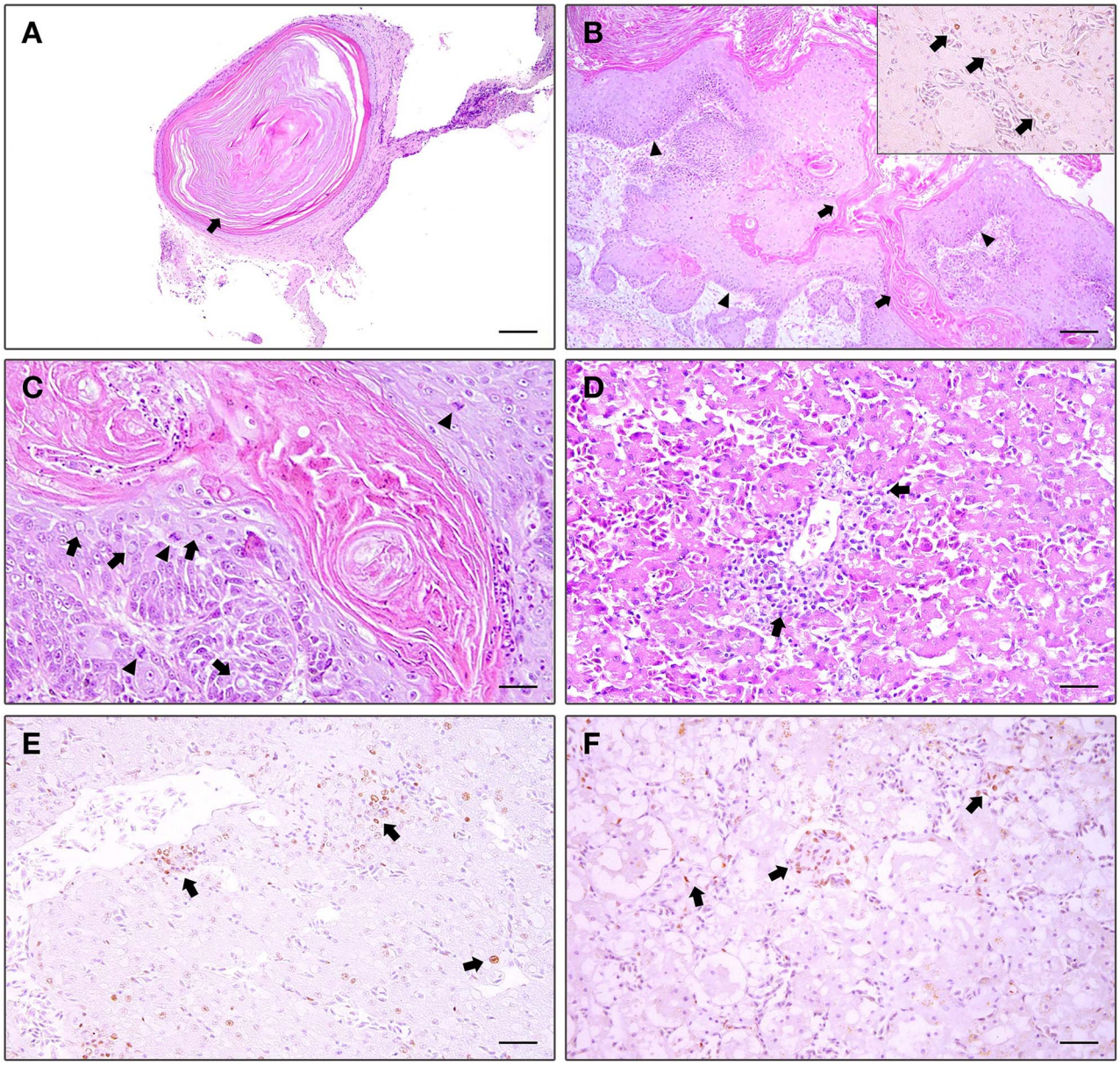

Figure 2. Histopathology from a 24-year-old saker falcon (*Falco cherrug*) with a keratoacanthoma of the uropygial gland. (A) A compact, cystic mass consisting of typical oval-elongated lamellae caused by altered keratinization. The result is a cystic mass filled with keratin, various cells, and amorphous fragments. Note the characteristic stratified aspect of the keratin in concentric circles (arrow) that merge into an amorphous material in the central area of the cyst (hematoxylin and eosin; bar = 1000 μm). (B) Neoplastic area of the uropygial gland, showing atypical proliferation of keratin and squamous cell layers, consistent with an infiltrating keratoacanthoma. Note the typical aspect of the tumor, characterized by a crateriform structure, filled with keratin, and basal cell proliferation (arrows), producing a generally well-delineated interface between the tumor and underlying subcutaneous tissue (arrowheads) (hematoxylin and eosin; bar = 500 μm). Immunohistochemistry results showed positive detection of anti-infectious laryngotracheitis virus (ILTV) antigen in some neoplastic epithelial basal cells from the uropygial keratoacanthoma (arrows) (insert ×60). (C) Area of the tumor characterized by intra-lesional cell proliferation, with mostly well-differentiated epithelial cells. Mitoses, mostly typical, were observed mainly in the basal layer of the epidermis (arrowheads). Squamous cells with abundant central cytoplasm and a lack of significant atypical cellularity; keratin whorls are evident in the central part of the field. Note the presence of amphophilic endonuclear inclusions in scattered neoplastic cells of the basal layer of the tumor (arrows) (hematoxylin and eosin; bar = 100 μm). (D) Diffuse vacuolar-hydropic degeneration and swollen hepatocytes. Note a focal perivenous area of mononuclear cells infiltration (arrows) (hematoxylin and eosin; bar = 250 μm). (E) Immunohistochemistry results showing positive ILTV antigen detection in some intranuclear hepatocyte inclusions (arrows) (immunohistochemistry; bar = 200 μm). (F) Immunohistochemistry results showing positive ILTV antigen detection in some glomerular and endothelial cells of the kidney (arrows) (immunohistochemistry; bar = 200 μm).

with thermoregulation, impaired preening, and secondary health complications. Diseases of the uropygial gland include adenitis, impaction, abscessation, hyperplasia, metaplasia, hyperkeratosis due to vitamin A deficiency, cyst formation, trauma, and neoplasia.[6–9] Impaction of the uropygial gland and uropygial gland disease are generally less common in raptors than in other bird species.[10] Gland impaction in this saker falcon follows those characterized in the literature, including enlargement of the gland, dry wick feathers, obstructed ducts, a hardened plug, hyperkeratotic lesions, and fistulous tracts.[8,9]

Previous reports of uropygial gland neoplasms include adenomas, carcinomas (eg, squamous cell carcinoma), papillomas, and epitheliomas.[5,6,8,11,12] Histopathological examination of this falcon's uropygial gland found an atypical proliferation of keratin consistent with an infiltrating KA, a common yet underreported cutaneous tumor characterized by rapid growth.[6,13] In the past, KA has been considered squamous cell carcinoma, and its designations have been used interchangeably; however, KA should be regarded as a distinct neoplasm with a distinct clinical course.[6,13–15] Macroscopic features cannot distinguish between KA and squamous cell carcinomas, and diagnosis should be based on clinical and pathologic features.[13] Rare cases of KA have evolved into squamous cell carcinomas or exhibit malignant behavior; however, this distinction poses a challenge on a clinical level, from a correct histopathologic diagnosis to appropriate treatment management.[6,13,15] Keratoacanthomas are typically described as skin nodules or crater-like ulcers in broiler chickens, although they have also been reported in other species, including budgerigars.[13,14,16,17] Petrak et al[18] reported a KA in the uropygial gland of a budgerigar, but to the authors' knowledge, this is the first description of a KA in a bird of prey.[18] The pathogenesis of KAs may be influenced by various factors, including trauma, foreign bodies, chemicals, and radiation.[13] In the case reported here, it is possible that there was recurrent infection and traumatization of the uropygial gland that may have further contributed to the development of the KA. Moreover, immunosuppression may play a significant role in KA pathogenesis, for example, due to viral infections.[15,17,19] Immunohistochemistry analysis in this falcon confirmed the presence of ILTV antigens in the examined tissues, along with pathognomonic hepatic inclusion bodies. Although molecular testing to identify the specific type of virus was not possible, recent taxonomic updates confirm that the *Gallid alphaherpesvirus 1* (ex-ILTV) belongs to the same clade as the falconid herpesvirus (*Falco tinnunculus alphaherpesvirus 1*).[20]

Avian herpesviruses are widespread in both captive and free-ranging raptors, including falcons, and can affect birds of all ages.[9,21,22] Herpesviruses may cause lifelong latent infections with intermittent viral shedding; however, acute fatal infections have also been reported. Affected birds are presented with clinical signs such as anorexia, vomiting, depression, and green-colored urates.[9,22] Antemortem diagnosis is often challenging because of the rapid progression of the acute form of disease or because latent infections are generally asymptomatic.[9,22]

The term "falcon herpesvirus infection" remains controversial. A study by Gailbreath and Oaks,[23] which examined herpesvirus isolates from falcons and pigeons, concluded that Falconid HV-1 and Columbid HV-1 are the same virus and are responsible for inclusion body hepatitis, proposing that the virus be solely referred to as Columbid HV-1. However, in 2018, a novel alphaherpesvirus was also isolated from a great horned owl (*Bubo virginianus*) and referred to as Strigid Herpesvirus 1 (StrHV1).[24] Although the clinical, gross, and histopathologic presentations of the disease in raptors are similar to those observed in pigeons, further research is needed to better understand its transmission and epidemiology in raptors.[23] Horizontal transmission through ingestion of infected pigeons has been documented, but it is also suggested that falcons may contract the virus via ocular or nasal routes.[21]

The IHC findings across multiple organs suggest systemic viral replication and a generalized infection.[25] Additionally, the hepatic and splenic lesions observed are typical of acute viral infections, including herpesvirus, with splenic white pulp depletion potentially linked to severe immunosuppression. Finally, microvasculitis with fibrinoid necrosis was observed at the capillary level. This phenomenon was attributed to viral tropism for the endothelium, as evidenced by IHC findings, and because of complement activation due to the deposition of immune complexes. This process reflects a type III hypersensitivity reaction, which ultimately led to a bleeding diathesis.

This case highlights the importance of clinicians being vigilant in identifying all disease conditions that may be affecting an avian patient at the time of presentation. By identifying all potential disease problems, a diagnostic and treatment plan can be established to obtain a rapid recovery, or an educated prognosis can be made regarding the bird's ability to recover.

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