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## **A chronic, non-healing, ulcerative and proliferative lesion revealed to be squamous cell carcinoma in a camel**

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**CASE REPORT**

Zoo animals

# A chronic, non-healing, ulcerative and proliferative lesion revealed to be squamous cell carcinoma in a camel

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**Abstract**

A 20-year-old, male, neutered camel presented with an 8-month history of a proliferative and ulcerated cush pad lesion refractory to topical wound management. The referring veterinarian performed a punch biopsy to further investigate the tissue; findings were consistent with granulation tissue. The patient was referred to University of Tennessee Farm Animal Medicine and Surgery service for additional diagnostics, surgical debridement and intensive wound care. The camel underwent surgical debridement of the lesion, and histopathology was consistent with a squamous cell carcinoma. Bloodwork revealed a severe non-regenerative anaemia and leukocytosis suspected to be paraneoplastic changes. During hospitalisation, it was identified that the patient suffered from a subluxated fetlock of the left front limb and a fully dropped fetlock of the front right limb due to compensatory over-weightbearing. Due to poor prognosis of the aggressive squamous cell carcinoma associated with a severe anaemia and concomitant musculoskeletal disease, humane euthanasia was elected.

**BACKGROUND**

There is a paucity of information specifically related to cush pad wound management in camels.<sup>1</sup> These wounds represent a welfare challenge as they immediately impair the comfort of the animal while resting, and ultimately can lead to gait abnormalities.<sup>2,3</sup> Recognising the possibility of a more extensive disease process due to limited wound healing after appropriate treatment is key when contemplating referral to a tertiary clinic. Proper tissue sampling of diagnostic quality is important to make this decision.<sup>4</sup> Especially as early diagnosis of neoplastic diseases is imperative to result in the best outcome, and a poor prognosis may limit an owner's willingness to pursue further treatment.<sup>5</sup>

This case presents a learning opportunity in the investigation and approach to treating a chronic, non-healing wound that through diagnostic evaluation was identified as cutaneous squamous cell carcinoma (SCC) with suspect paraneoplastic syndromes. Currently, there is limited knowledge in camels regarding metastasis and paraneoplastic syndromes caused by SCC. The investigative steps performed before surgery in this case can be applied to any species of domestic animals and performed at most primary care veterinary hospitals.

**CASE PRESENTATION**

A 20-year-old, male, neutered, dromedary camel was referred to the University of Tennessee College of Veterinary Medicine's Farm Animal Medicine and Surgery (UT FAMS)



**FIGURE 1** Gross image of cush pad lesion before surgical debridement. The skin is ulcerated, proliferative and purulent with a fetid odour. The cranial aspect of the patient is to the left of the image and caudal is to the right, left lateral is at the top of the image, while right lateral is at the bottom

with the presenting complaint of a chronic, non-healing proliferative and ulcerated wound on its cush pad (Figure 1). The wound was first noted 8 months before presentation. The patient was reported to frequently self-mutilate this lesion with its mouth and feet. The wound was being treated topically by the referring veterinarian with an ointment containing a mixture of a steroid, desitin and nitrofurazone. The owner attempted to prevent further self-mutilation by

applying a wrap to the lesion. Unfortunately, no improvement was observed with the wrap or topical treatment. A punch biopsy was performed on the refractory wound, which revealed granulation tissue interpreted to be exuberant proud flesh. The patient was then referred to UT FAMS for surgical debridement of the granulation tissue, more intensive wound management and further diagnostic investigation of the lesion.

Upon presentation to UT FAMS, the patient was bright, alert and responsive, had normal appetite and thirst, and had no significant medical history. Heart rate was increased at 72 beats per minute, but other vital parameters were within normal limits. A 32.5 × 15.5 cm wound was present at the ventral aspect of the cush pad. The wound bed was filled with a red irregular and proliferative tissue exceeding the level of the skin at the margins of the wound by 2–5 cm. The wound was constantly draining, and a fetid odour was present. It was noted during initial workup that both pre-scapular lymph nodes were irregularly enlarged (left larger than right), firm and multilobulated. The patient also had a 4 × 4 × 2 cm single, firm, pedunculated mass present on the caudo-ventral abdomen, 6 cm to the left of the prepuce.

No gait abnormality was noticed upon arrival. However, a dropped right fetlock was present and attributed to the age of the patient.

## INVESTIGATIONS

Radiographs of the cush pad lesion were taken to investigate the integrity of the underlying bones and to rule-out the presence of radio-opaque foreign bodies or osseous sequestrum. Right lateral views of the cush pad revealed a well-defined, round, lobular, heterogenous soft tissue mass, ventral to the thorax and caudal to the elbow, measuring 32.5 × 15.5 cm. The lesion had irregular ventral margins and contained dissecting round to linear gas opacities. The ventral margin of the sternum, dorsal and adjacent to the soft tissue mass, was irregular with the impression of new, smooth, lamellar periosteal bone production. No abnormalities were noted on the sternbrae.

Following radiographs, the patient underwent surgical resection of the cush pad lesion and the preputial mass, both of which were submitted for histopathology (see Treatment section).

Intraoperative blood was drawn for a complete blood count (CBC) and chemistry panel. The camel had a haematocrit of 9% (normal range 24%–35%,  $M \pm SD$ :  $30 \pm 5$ ).<sup>6</sup> The CBC revealed a red blood cell count of  $3.10 \times 10^6/\mu\text{l}$  (normal  $7.6\text{--}11.0 \times 10^6/\mu\text{l}$ )<sup>6</sup> and a fibrinogen of 200 mg/dl (normal  $\leq 400$  mg/dl).<sup>6</sup> An additional CBC was also performed 4 days after operation, which revealed a fourfold increase in white blood cells, specifically segmented neutrophils;  $5.1 \times 10^3\text{--}21.61 \times 10^3/\mu\text{l}$  total white blood cells (normal  $11\text{--}16 \times 10^3/\mu\text{l}$ ,  $M \pm SD$ :  $13 \pm 2 \times 10^3/\mu\text{l}$ ),  $4.341 \times 10^3\text{--}19.441 \times 10^3/\mu\text{l}$  segmented neutrophils (normal range  $4.6\text{--}16 \times 10^3 \mu\text{l}$ ,  $M \pm SD$ : 50%).<sup>6</sup> The anaemia was non-regenerative based on blood smear examination. The chemistry panel was within normal limits.

A faecal float and egg count panel were performed following bloodwork results to rule out a gastrointestinal parasitic cause of the anaemia. Results showed moderate trichostrongyle eggs ( $\sim 200$  eggs per gram), likely not a severe

## LEARNING POINTS/TAKE HOME MESSAGES

- When considering biopsy for a large, proliferative or non-healing wound, it is important to ensure you have a deep enough tissue sample for diagnostic results.
- Geriatric camels, like other animals, are expected to develop age-related medical conditions such as cancer and musculoskeletal abnormalities, making it important to examine them regularly to identify signs of disease early when there are likely more treatment options available.
- When a conversation regarding the possibility of humane euthanasia due to quality-of-life concerns is reached with the owner about their animal, it is important to take into consideration all ongoing comorbidities and long-term prognosis even with aggressive treatment when making this decision.
- Paraneoplastic syndrome of haematologic parameters, particularly anaemia, and neutrophilic leukocytosis unresponsive to antibiotic treatment, may manifest before or during clinical disease and can be helpful findings when interpreting a lesion as neoplastic or not pending biopsy results.

enough burden to cause the severity of anaemia seen in the patient.

Histopathology of the cush pad lesion was consistent with SCC. The neoplasm consisted of multiple islands and trabeculae of epithelial cells with moderate atypia. Islands of neoplastic cells had central keratinisation (keratin pearls), surrounded by desmoplasia. There were many areas of necrosis within the tumour and the epidermis was ulcerated. The tumour extended into the margins of the tissue samples submitted. Histopathology of the smaller, pedunculated preputial mass was consistent with a poorly differentiated sarcoma.

Pending the histological results, it was noticed that the patient regularly stood with his left front foot crossed over his right. As such, an investigation into the patient's musculoskeletal system was performed. A lameness exam was performed, and it appeared that he was favouring his left front limb over his right. Radiographs were performed on both front distal limbs, which showed a medial subluxation of the metacarpophalangeal joint on the left front foot as well as a severe hyperextension of the metacarpophalangeal joint, resulting in a plantigrade stance of the right foot.

## DIFFERENTIAL DIAGNOSIS

No specific history of trauma was present for this camel. However, the presence of a non-healing wound concomitant with a proliferative granulation tissue suggested the possible continuous presence of a non-healing wound of idiopathic origin due to self-mutilation, the presence of a persistent foreign body or bone sequestrum on the caudal sternbrae, pythiosis or a neoplasia.

## TREATMENT

Surgical debridement of the cush pad lesion was performed with the camel positioned in right lateral recumbency under general anaesthesia. One subcutaneous dose of 6.6 mg/kg of ceftiofur crystalline-free acid (Excede, Zoetis, Parsippany-Troy Hills, NJ, USA) and 1.1 mg/kg intravenous flunixin meglumine (Prevail, VetOne MWI Veterinary Supply, Meridian, ID, USA) were administered intraoperatively. Sharp debridement of the edges of the exuberant tissue at the periphery of the wound was performed using a #10 blade so that the wound bed would be below the skin level. Once the edges of the lesion had been resected, large superficial sections of the mass were excised in a piecemeal fashion. Mild bleeding was controlled with electrocautery and vessel ligation. It was suspected that the proliferative tissue extended deeper, but given the surface of the wound and the achievement of sufficient debridement to eliminate the superficial infection present, surgical excision was deemed sufficient to initiate a secondary healing process.

Stay sutures were placed around the circumference of the wound using loops of #3 polyamid suture material (Braunamid; Braun), approximately 3–5 cm away from the wound's edge in preparation for a tie-over bandage. After haemostasis was achieved, the surgical site was bandaged using sheets of calcium alginate dressing with active *Leptospermum* honey (Medihoney; Derma Sciences) in direct contact with the wound surface, followed by a thick layer of Kerlix gauze (Kerlix; Covidien), followed by two huck towels, followed by an absorbent layer (Xtrasorb Super Absorbent Dressing), and finished with two more huck towels. Umbilical tape was used to close the tie-over bandage and keep the layers of bandage material firmly in place.

Near the end of the surgery on the cush pad mass, the second smaller mass present on the caudo-ventral abdomen 6 cm to the left of the prepuce was clipped and prepped. This superficial, pedunculated mass was removed using a #10 scalpel blade. The skin incision was closed with #1 polyamid suture material (Braunamid; Braun) suture in a single simple continuous pattern.

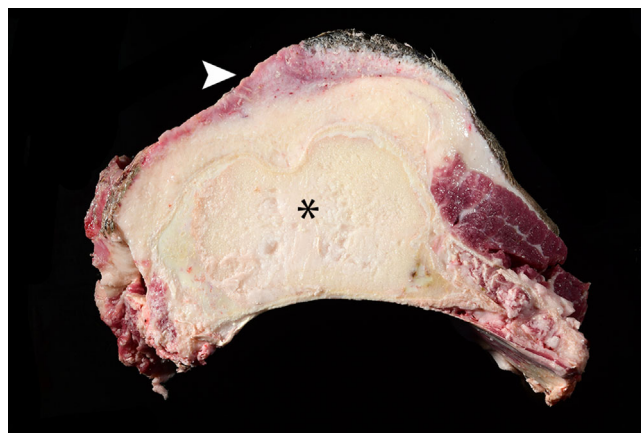
The camel recovered from surgery and general anaesthesia without complication.

The bandage over the cush pad wound was replaced in an identical fashion 3 days after operation. The wound bed appeared less inflamed and smoother.

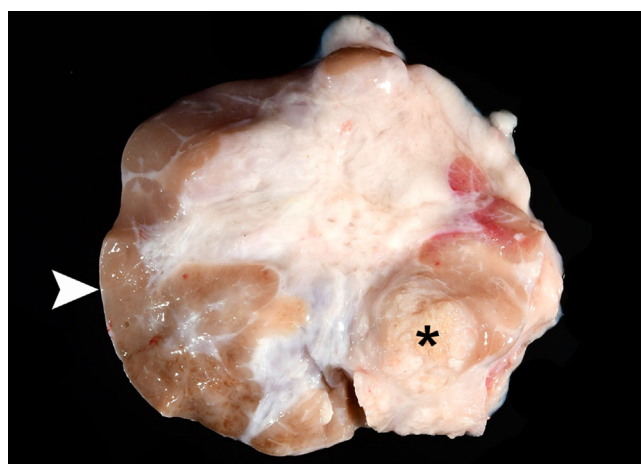
## OUTCOME AND FOLLOW-UP

The histopathological evaluation of the excised masses revealed an SCC of the cush pad and undifferentiated sarcoma affecting the left side of the prepuce. With the finalised histopathology, the owners elected humane euthanasia of the patient due to poor prognosis, possible metastasis to the local lymph node, musculoskeletal comorbidities, and suspect paraneoplastic anaemia and leukocytosis. A post-mortem examination was performed to investigate the extent of disease.

Postmortem examination corroborated cutaneous SCC of the cush pad. The sternum was transversely sectioned and the mass penetrated up to 3 cm into the subcutaneous adipose tissue, but not the sternal bone (Figure 2). The extent of metastasis was limited to the right pre-scapular lymph node (Figures 3



**FIGURE 2** Transverse section of the sternum at the level of the cush pad. The skin is ulcerated (arrowhead) and the mass infiltrates into the subcutaneous tissue. The neoplasm does not extend to the sternal bone (asterisk)



**FIGURE 3** Right pre-scapular lymph node. The lymph node is enlarged, multinodular and contains a well-demarcated semi-firm white-tan mass filled with gritty material (asterisk). Remaining lymphoid follicles are pushed to the periphery of the lymph node (arrowhead)

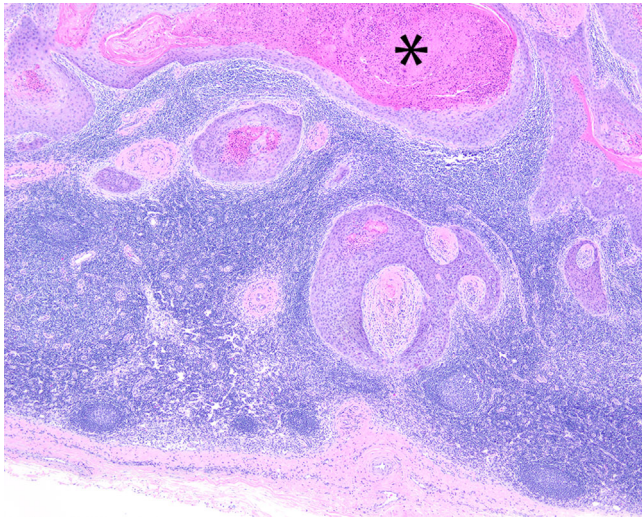
and 4). There was moderate erythroid hypoplasia in a rib sample of bone marrow. The degree of erythropoiesis was considered insufficient in the face of anaemia, and the absence of iron storage suggested iron deficiency. Postmortem examination also confirmed severe degenerative joint disease in both front fetlocks.

## DISCUSSION

Though cases of SCC in camels have been described,<sup>7,8</sup> this report is the first description in a camel of SCC of the cush pad with suspect paraneoplastic syndromes. To the authors' knowledge, no reports of haematologic paraneoplastic syndromes have been reported in camels previously.

Tumour distribution by organ among camels in Saudi Arabia and Egypt include most frequently the limbs, vagina, abdominal wall and head,<sup>6</sup> with most common location of cutaneous SCC on abdominal wall.<sup>7</sup> Though SCC has similar risk factors across species, including exposure to ultraviolet radiation and age,<sup>9</sup> camels in the northern latitudes likely are exposed to different risk factors than in their native habitats.





**FIGURE 4** Histopathologic image of the right pre-scapular lymph node. Islands and anastomosing trabeculae of neoplastic epithelial cells with central keratinisation (asterisk) infiltrate and partially distort the lymph node architecture

Therefore, it is critical to evaluate cutaneous lesions with a systematic fashion of diagnostics and treatments, while also keeping in mind the camel's history and environmental risk factors.

SCC of the digits in camels from the Middle East are common and described to start as a solid, raised skin mass that if not addressed, expands to surrounding soft tissue structures and becomes ulcerative with proliferative granulation tissue.<sup>9,10</sup> The patient described in this report presented at the chronic stage of ulceration and exuberant granulation tissue in addition to pre-scapular lymphadenopathy. The referring veterinarian treated the patient before presentation and, in routine method because the wound was unresponsive to treatment, performed a punch biopsy. Results were supportive of proliferative granulation tissue. The patient was subsequently referred for exuberant fibrous tissue evaluation at UTCVM. Large animal veterinarians often treat exuberant granulation tissue in horses, which can present in a similar manner.<sup>11,12</sup> Thus, cutaneous proliferations may present as a pretence in cases of neoplasia if biopsy results are too superficial. Pythiosis (*Pythium insidiosum*) can also present similarly and has previously been diagnosed in two camels in Tennessee afflicting their vulvar regions.<sup>13</sup> The cases presented as eosinophilic dermatitis following two biopsy evaluations. However, definitive diagnosis was deemed to be *Pythium* after both camels underwent surgical debulking and repeat histopathology and culture could be performed. Because of this case report, pythiosis was also a differential in the case presented here but ruled out on postoperative histopathology. In cases of large, ulcerative, non-healing wounds as seen here, it may be best practice to perform either a wedge biopsy or a surgical biopsy (either elliptical or excisional depending on size), as punch biopsies may not be representative of deeper tissue that have more obvious signs of neoplasia on histopathology.<sup>14</sup>

A noteworthy similarity to previously published reports of SCC in camels and this report is the prolonged history and unresponsiveness to conventional treatment. A study out of Egypt classifying external tumours of dromedary camels showed that the majority of tumours were noticed 4 months to 2 years before presentation, with most of them presenting

between 12 and 18 months after initial onset.<sup>7</sup> In one case, the camel had a 9-month history of proliferative cutaneous wound with a granulomatous appearance on the fetlock and progressive lameness, which were unresponsive to unspecified conventional treatment.<sup>15</sup> In another report of a camel with SCC of the foot, the patient presented with a 12-month history of exuberant granulation tissue on the sole of the foot that was fragile and tended to bleed.<sup>16</sup> The camel in the present case report had a chronicity of 8 months before referral to a tertiary hospital. Not only does prolonging appropriate, targeted treatment present a welfare concern for these camels, it also may decrease the prognosis with treatment. Increased time to presentation for clinical intervention can be concerning if a lesion is diagnosed as SCC, as the longer it persists the more likely it is to invade surrounding tissues and metastasise. Aggressive surgical intervention in combination with adjunctive therapy early in the disease process is associated with best prognosis in cutaneous SCC of other domestic species, including dogs, cats, goats, horses and sheep.<sup>17–20</sup>

Another similarity between other cases of neoplasia in camels and the one presented here is that despite the obvious lesions they present with, they are reported to be bright, alert and responsive with minimal systemic signs of illness at presentation. Examples include a camel with mammary and pulmonary carcinoma with swollen mammary glands managed at a zoo<sup>21</sup> and a camel with 10-month chronicity of an oral SCC.<sup>22</sup> If owners are unable to observe obvious signs of pain or lameness, this may cause prolongation of presenting camels with lesions to veterinarians. As in the case described here, the camel presented for the obvious large cush pad lesion, but due to its seemingly normal behaviour, appetite, thirst, urinations and defecations, its severe front limb musculoskeletal abnormalities went unintentionally overlooked 3 days into hospitalisation. Signs of discomfort in the patient were minimal other than laying in an abnormal, not quite sternal, recumbency to avoid putting pressure on its cush pad. Its most obvious sign of irritation was regularly self-mutilating the wound. This stoic behaviour, though encouraging to owners and clinicians, may mask the severity of the ongoing disease and highlights a need for techniques of evaluating pain and lameness in camels similar to those published for cattle,<sup>23</sup> horses<sup>24</sup> and pigs.<sup>25</sup> Appropriately evaluating an animal's behaviour and welfare of any species is of the utmost importance in veterinary medicine. The better we can assess pain and lameness in camels, the better we are able to evaluate and manage their discomfort as well as attempt to understand the extent of ongoing disease processes.

Paraneoplastic syndromes have been described in humans and domestic animal species.<sup>26,27</sup> The camel here had persistent anaemia of unknown origin, which may have been a paraneoplastic consequence related to the SCC. The anaemia was non-regenerative on cytologic evaluation, and no clear pathogenesis could be identified on histopathology. The patient did not have any apparent on-going blood loss and its parasite load was relatively low at 200 eggs per gram of faeces.<sup>28</sup> Therefore, the most plausible cause would be a paraneoplastic anaemia due to erythroid hypoplasia and iron deficiency recognised on postmortem examination. Other potential causes of the bone marrow erythroid hypoplasia include chronic infection or inflammation as seen in this case (though unlikely as the fibrinogen was within normal limits).<sup>29</sup> There is also the possibility it had a paraneoplastic neutrophilic leukocytosis

developing, which has been described in dogs<sup>30</sup> and cats<sup>31</sup> because the patient's white blood cell count, specifically neutrophils, increased fourfold before to after operation in the face of antimicrobial therapy. Another potential cause of the neutrophilic leukocytosis includes an increase after operation from a surgical site infection, which would cause local inflammation to the area of the wound, or a mild aspiration pneumonia from postoperative regurgitation, following extubation of the endotracheal tube after surgery. However, this is less likely as the patient did not have any clinical signs of aspiration during hospitalisation postoperatively.

SCCs are malignant neoplasms of squamous epithelial cells that are commonly slow growing but locally infiltrative into surrounding soft tissue and regional lymph nodes. Recurrence, regional malignancy, local invasion and paraneoplastic syndromes are known consequences associated with numerous types of neoplasia.<sup>17–20,30–32</sup> Applying knowledge from literature published from their native environments while including their current environmental risk factors, such as age and sunlight exposure, are all important aspects of a camel's veterinary exam. Performing a complete physical exam, gait evaluation, diagnostic bloodwork and taking deep biopsy samples can help diagnose neoplasia like SCC early, increasing treatment options and potentially improving prognosis.

## CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

## FUNDING INFORMATION

This report did not receive any funding. Case information was reviewed and reported in a retrospective fashion.

## ETHICS STATEMENT

This case report includes detailed information from medical records while maintaining client and patient confidentiality. The animal described was client owned and consent was provided by the client to report the case. No specific institutional or national ethical committees oversaw the reporting of this case, as case information was reviewed and reported in a retrospective fashion.

## AUTHOR CONTRIBUTION

JG investigated case information, wrote, edited and revised the original and final drafts of the manuscript. EM compiled and organised case information and assisted with writing and editing the manuscript. CMCA and AC contributed expertise regarding the anatomic and histologic pathology findings of the case, as well as wrote and edited these sections of the manuscript. PYM provided oversight and leadership for the reporting, assisted in writing and editing and was fundamental in conceptualisation of the manuscript.

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