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CLINICAL MANAGEMENT OF BILATERAL CUTANEOUS SQUAMOUS CELL CARCINOMA OF THE HIND FEET PADS IN A SOUTHERN WHITE RHINOCEROS (*CERATOTHERIUM SIMUM SIMUM*)

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Abstract: The current report describes the temporary regression, due to intensive symptomatic treatment, of ulcerative skin lesions caused by squamous cell carcinoma in a white rhinoceros. A captive, 40-yr-old southern white rhinoceros (*Ceratotherium simum simum*) developed profound, ulcerative skin lesions on the pads of both hind feet. At the peak of the disease, at least one quarter of the pads was affected. A diagnosis of squamous cell carcinoma was made via biopsy. Treatment included anti-inflammatory drugs, antibiotics, and local care. The lesions regressed on both feet until they seemed clinically healed. It was presumed that long-term, anti-inflammatory treatment and local bandaging had induced the temporary regression of the lesions. Two years later, however, a small ulcerative lesion reappeared on one pad and post mortem examination confirmed that the carcinoma was also histologically present in the clinically intact tissue. No metastasis was found and computed tomography showed normal digital bones.

Key words: *Ceratotherium simum simum*, foot pad, imaging diagnosis, regression, squamous cell carcinoma, white rhinoceros.

BRIEF COMMUNICATION

Only a few malignant skin tumors in rhinoceroses have been described.[1,8,13] Specifically, squamous cell carcinoma has been described three times: Once in an Indian rhinoceros (*Rhinoceros unicornis*) where the carcinoma appeared at the base of the horn and twice in southern white rhinoceroses (*Ceratotherium simum simum*), once on the hind foot and once on the flank.[3–5,7]

A captive, 40-yr-old female southern white rhinoceros, weighing approximately 1,700 kg, would not bear full body weight on its left hind foot when standing and had a mild lameness. A 3.5 cm–diameter ulcerative skin lesion was detected on the caudo-medial part of the foot pad. Local, oral anti-inflammatory and antibiotic treatment over 2 mo did not improve the animal's condition; therefore, further investigation under general anesthesia was performed. The inspection showed one ulcerative, caudo-medial wound on each hind foot pad, the right skin lesion measuring 2 cm in diameter and the left skin lesion having increased since discovery to 7 cm in diameter.

Punch biopsies of four different areas of the ulcerative skin lesions of the right foot pad were taken. Histology revealed a poorly delimited, densely cellular, invasive epithelial neoplasm composed of polygonal cells arranged into anastomosed cords and islands with central keratinization, located within the dermis (Fig. 1A). Cells were supported by an abundant, densely collagenous, well vascularized desmoplastic stroma. Individual polygonal cells had abundant homogenous eosinophilic cytoplasm with distinct cellular borders and prominent intercellular bridges. Nuclei were round with coarsely clumped chromatin and a prominent magenta nucleolus. Anisocytosis and anisocaryosis were moderate and mitotic figures were rare, with five mitoses per 10 random fields at ×400. No evidence of vascular invasion was noted. Marked suppurative inflammation was present within the mass and the surrounding dermis. The surface of the mass was ulcerated and colonized by numerous cocci.

Management of the wounds consisted of the oral administration of intermittent to long-term anti-inflammatory drugs and antibiotics when secondary infection occurred (Table 1). Intensive daily local wound care was additionally performed for months until the wounds resolved. The local care involved wound cleaning and bandaging of the feet with large, absorbent cotton

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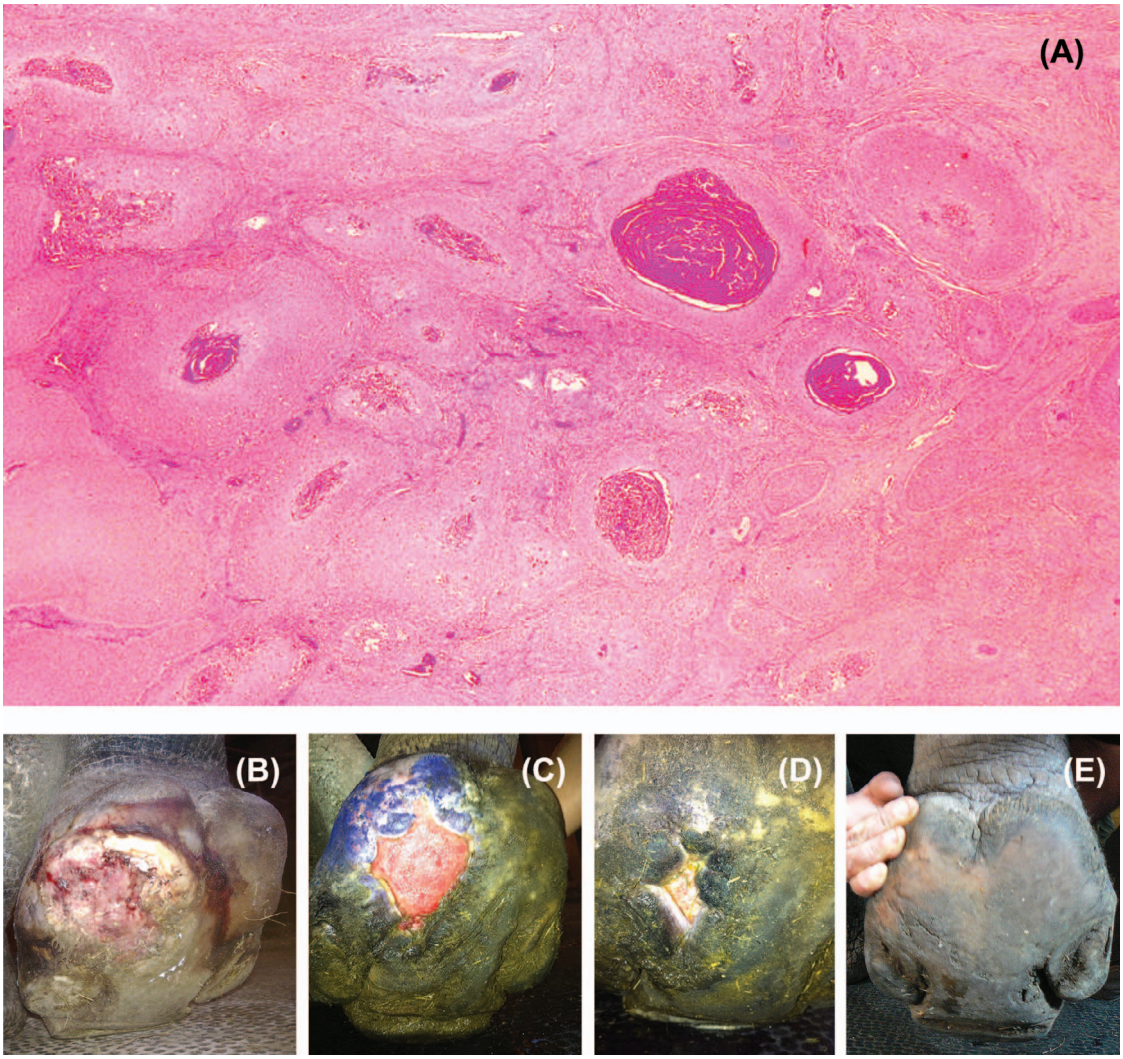

Figure 1. **A.** Histologic section of the cutaneous squamous cell carcinoma of the hind foot pad, *Ceratotherium simum simum*. Image shows the epithelial neoplasm composed of polygonal cells arranged into anastomosed cords and islands with central keratinization, supported by abundant desmoplastic stroma. H&E stain. ×2. **B–E.** Ulcerative skin lesion of the right hind foot pad caused by squamous cell carcinoma, *Ceratotherium simum simum*. Regression of the wound over a period of 9 mo due to intensive symptomatic treatment and wound management.

pads to increase hygiene and comfort of the animal. The lesions on both hind feet were intermittently secondarily infected and bleeding, and the right distal foot had temporary abscess formation. The products for local care changed depending on the wound aspect.

During the initial 6 mo of treatment, the left hind foot lesion increased to one quarter of the foot pad. Under continued treatment the lesion regressed and complete healing of the pad was noted after 1 yr. Eighteen months after clinical resolution, a skin ulcer reappeared in the same region, increasing in size to 3 cm in diameter. It did not heal despite local treatment and the animal was euthanized 6 mo later.

The wound on the right hind foot pad had remained stable for 6 mo following examination but then increased in size, so treatment was instituted as well. During the subsequent 15 mo, the wound increased until one third of the pad was ulcerated. After this, granulation tissue started to form and the skin ulceration resolved at 9 mo (Fig. 1B–E). Until euthanasia was performed, the foot pad remained clinically healthy.

The animal was euthanized 4 yr after the detection of the first lesion due to increased

Table 1. Clinical management of bilateral ulcerative skin lesions of the hind feet pads caused by squamous cell carcinoma (*Ceratotherium simum simum*). Overview of the main medications and supplies used for oral and local treatment.

Treatment	Drug	Dose (mg/kg) frequency	Administration	Duration (days)	Drug name and manufacturer	Additional Information
Anti-inflammatory drugs	Phenylbutazone	5 b.i.d. × 1 day; 2.5 b.i.d. × 4 days; 2.5 s.i.d. × 5 days	Oral	10	Equipalazone, Dechra Veterinary Products SAS, 92150 Suresnes, France	9× in total
		1.7 s.i.d. every second day	Oral	328	Equipalazone, Dechra Veterinary Products SAS, 92150 Suresnes, France	Low dose every second day until the ulcerative skin lesions started to decrease in size
Antibiotic drugs	Amoxicillin	14 s.i.d.	Oral	5	Suramox 10,Virbac France, 06511 Carros, France	4× in total
	Sulfamethoxypyridazine and trimethoprim	20 s.i.d	Oral	10–25	Avemix n° 150, Vetoquinol S.A., 70204 Lure Cedex, France	11× in total
	Flumequin	5.7 b.i.d.	Oral	10	Flumiquil; CEVA Santé animale, 33500 Libourne, France	1×
Local care left foot	Malic acid, benzoic acid, salicylic acid		Topical	124	Dermaflon Solution; Zoetis France SAS, 75668 Paris Cedex 14, France	Solution for wound cleaning and debridement
	Malic acid, benzoic acid, salicylic acid		Topical	93	Dermaflon crème; Zoetis France SAS, 75668 Paris Cedex 14, France	Cream to cover absorbent cotton pad to support wound debridement
Local care right foot	Chlorhexidine 1%		Topical	365	Hibitane 5%, MSD Santé Animale, 49071 Beaucouze Cedex, France	Antiseptic solution, wound cleaning
	Chlorhexidine spray		Topical	365	Cicajet 18, Virbac France, 06511 Carros, France	Absorbent cotton pad moisted with chlorhexidine spray
Bandaging			Topical	Left foot : 93 right foot : 465	Absorbant cotton pad 15 × 20 cm; Pansements RAFFIN; 69490 Saint Romain de Popey, France	Bandaging the foot after local wound care with an absorbent cotton pad, minimum once a day

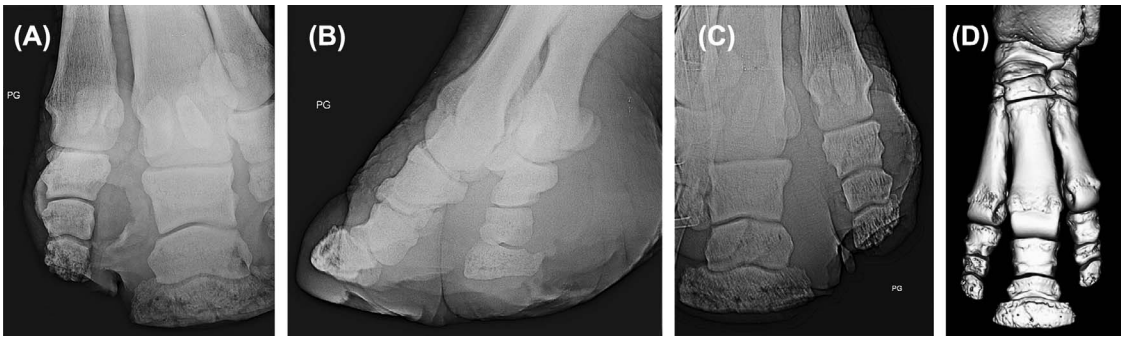

Figure 2. Radiographic and computed tomographic imaging of the left hind foot from a southern white rhinoceros (*Ceratotherium simum simum*) diagnosed with cutaneous squamous cell carcinoma of the hind feet pads. **A–C.** Antemortem radiographic projections depict normal distal metatarsal and phalangeal bone anatomy. **D.** Postmortem computed tomographic images confirm that tarsal, metatarsal, and phalangeal bone structures of the foot are within normal limits and unaffected by the underlying soft tissue tumor. PG = left hind foot.

ataxia and weakness in the hind legs and the known presence of uterine masses diagnosed 9 mo earlier via ultrasound. Histology confirmed the bilateral squamous cell carcinoma, both on the ulcerative skin lesion on the left foot pad and on the clinically intact right foot pad.

Squamous cell carcinomas are malignant, locally invasive neoplasms with slow metastatic potential.[9,12] Therefore, surgical removal of the mass is recommended. This was performed successfully once, without remission for 2 yr, on the flank of a southern white rhinoceros.[5] In that case, the removal of the skin tumor on either foot pad was not possible, considering that the body weight of a rhinoceros is mainly carried on the feet and the extension of the carcinoma in the deep dermis was unknown.

Computed tomographic (CT) and radiographic examinations can help to investigate tumor dimensions, detect possible metastasis, bone involvement, and find unrelated bone pathology.[3,4] Antemortem analog radiographic (AR) and postmortem CT examinations were performed. AR examination was performed on the hind feet using a mobile X-ray unit (Poskom 20HF, Poskom, Korea; 70 kV, 6.4 mAs). CT data were acquired from all four feet using a high-resolution, 640-slice CT scanner (Aquilion ONE, Toshiba Medical Systems Corporation, Tochigi, Japan; 120 kV, 300 mA, 1 sec rotation time; Software: ViTREA Version 4.0 medical diagnostic software, Vital Images Inc., Minnetonka, Minnesota). Both high resolution and soft tissue reconstruction algorithms were used with 0.5-0.25 mm slice thickness-slice interval. Different AR projections and CT images showed tarsal, metatarsal, and phalangeal bones were within normal limits (Fig. 2). Furthermore, no soft tissue pathology of the feet pads could be diagnosed based on CT images.

Squamous cell tumors are common neoplasms in domestic species.[6,9,12] In cats (*Felis catus*), the most-commonly affected parts of the body are the ear and the nose, organs that are most exposed to ultraviolet (UV) rays.[9] In horses (*Equus ferus*), the tumors frequently develop in nonpigmented skin, which underlines the implication of UV light in the etiology.[12] UV light overexposure seems an unlikely etiology of such a tumor in the rhinoceros foot pad, as it is rarely exposed to UV light. Nevertheless, the foot pad is less pigmented than other body regions of the rhinoceros and is exposed to UV light when animals are recumbent. Viral infection with papilloma viruses have recently been associated with squamous cell carcinoma in horses and dogs (*Canis familiaris*), and there is one case report of a digital papilloma in a black rhinoceros (*Diceros bicornis*).[2,9,12] Chronic irritation is suggested to be another cause for squamous cell carcinoma development.[5,7,10] This could be due to hard substrate or, in this case, the female frequently sweeping the hind feet against one another when walking, causing chronic irritation on the same caudo-medial area of the feet pads where the ulcerative skin lesions appeared. Bandaging the ulcerative skin regions with large cotton pads protected the wound, reduced chronic irritation, and facilitated softer footing, thus supporting wound healing. Further research is needed to evaluate the potential role of UV light, viruses, or chronic irritation as causative agents for skin cancer in rhinoceroses.

Studies in human and veterinary medicine have shown that anti-inflammatory treatment, especially with cyclooxygenase-2 inhibitors, delays the

growth of cell carcinomas.[6,11,14] Phenylbutazone (Equipalazone, Dechra Veterinary Products SAS, 92150 Suresnes, France), a nonsteroidal anti-inflammatory cyclooxygenase inhibitor, was administered for more than 8 mo in this case. In addition to intensive wound management, it presumably had a positive effect on the regression of the lesions.

The superficial aspects of ulcerative, proliferating tumors can become infected with opportunistic pathogens.[12] Antibiotic treatment helped to limit secondary infections of the skin ulcers, which had an intermittent purulent aspect and abscess development. Daily cleaning of the wound and protective bandages played an important role in the limitation of secondary infections.

Surprisingly, the ulcerative skin lesions disappeared on both feet pads after long and intensive care whereas the carcinoma was still histologically present in the clinically normal skin. The intensive management of foot bandaging combined with long-term anti-inflammatory treatment and the limitation of secondary infections are assumed to have played a key role in the regression of the lesions caused by the tumor. Further research is needed regarding the etiology and the treatment of this malignant skin cancer in this species.

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