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Successful treatment of a squamous cell carcinoma in a white rhinoceros, *Ceratotherium simum*

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What is known about the topic of this paper
- Limited information as regard to this condition in Rhino's.

What this paper adds to the field of veterinary dermatology
- Surgical intervention is currative in some cases.
- Contributing to the sparse information on skin tumours in rhino's .

Abstract

A captive 33-year-old male white rhinoceros with seasonal dermatitis was diagnosed with a malignant squamous cell carcinoma on the right flank. *Staphylococcus aureus* was cultured from the skin lesions. No fungal or yeast was isolated. The dermatitis was treated with a combination of oral antibiotics (trimethoprim–sulphadiazine) and topically with weekly chlorhexidine washes and a mixture of a zinc oxide, balsam peru and bismuth oxide cream. Under azaperone and butorphanol anaesthesia, the skin tumour was surgically removed. The tumour was excised with wide margins and allowed to heal by secondary intention as primary wound closure was not possible. A post-mortem performed 2 years later for an unrelated condition revealed no metastases or recurrence of the skin tumour. It was presumed that chronic irritation or trauma may have contributed to the development of the skin tumour. This is the first detailed report of the successful treatment of a squamous cell carcinoma not associated with the horn in a rhinoceros.

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Introduction

The epidermis of the white rhinoceros is relatively thin with a thick and dense dermis. The epidermis is composed of approximately 5–10 layers of keratinocytes covered by several layers of cornified epithelial cells. The dermis is up to 2 cm thick.[1] Only a few reports have been published on skin neoplasia in rhinoceros in comparison to other causes of skin disease. Infectious causes of dermatitis most commonly described in this species include fungal,[2–4] bacterial[5] and Pox virus[1,6] infections. Other causes of skin disease are superficial necrolytic dermatopathy in black rhinoceroses,[1,7,8] epidermal exfoliation,[1,2] superficial pustular dermatitis,[1] eosinophilic dermatitis and granulomas.[1,8]

The only skin tumours reported to date in rhinoceroses tend to be malignant and locally invasive and following post-mortem no metastases have been found.[9,10] This includes a skin carcinoma removed from a white rhinoceros,[11] a squamous cell carcinoma (SCC) in an Indian rhinoceros[9] and a SCC of the horn.[10] Squamous cell carcinoma of the skin when not associated with the horn carries a good prognosis when surgically treated as described in this case. The purpose of this case report is to describe the successful treatment of SCC not associated to the horn in a rhinoceros.

Case report

A 33-year-old, wild caught, male white rhinoceros housed at Edinburgh Zoo, for the last 28 years, developed over a year, a nodular skin mass (approximately 1W × 2L cm) on the right flank (Fig. 1). During this period, it also developed a seasonal dermatitis that occurred in early summer as it had done the previous year. This presented as non-adherent scales along the dorsum exposing erythematous skin underneath.

Scales were submitted for both fungal and aerobic bacterial culture to rule out *Malassezia pachydermatis* and *Candida pachydermatis*.[2] Results of a fungal culture were negative. *Staphylococcus aureus* was isolated from the submitted scales, which was sensitive to the majority of antibiotics including amoxycillin/clavulanate, cephalexin, ciprofloxacin, cotrimoxazole, erythromycin and penicillin. *Staphylococcus aureus* has been isolated by others[7] and in this case is likely to be due to secondary infection. The rhinoceros had already started on a course of trimethoprim–sulphadiazine (Equitrim granules™, Boehringer Ingelheim Ltd; Bracknell, UK). The antibiotic treatment continued for a month in combination with topical treatment. Equitrim granules™ were administered at a horse dose for an estimated weight of 2000 kg. The rhinoceros was washed weekly by the keepers to remove epithelial and other debris using a chlorhexidine (Hibiscrub™ SSL International; Oldham, UK). A mixture of a zinc oxide, balsam peru and bismuth oxide cream (Anusol™, Pfizer Consumer Health Care; Eastleigh, UK) was applied to the skin. This combination of a soothing antiseptic and astringent cream had been used successfully at another zoo (personal communication). Emollients were applied to the dry areas of skin such as the paraffin- and lanolin-based cream (E45™,

Figure 1. Proliferative skin mass on the right flank of a white rhinoceros, *Ceratotherium simum*.

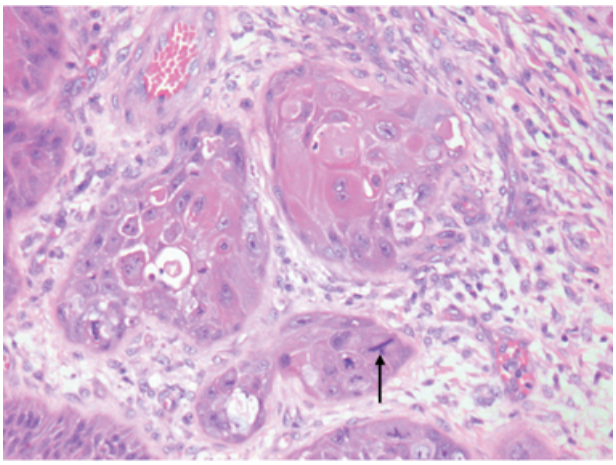

Figure 2. Islands of neoplastic squamous epithelial cells invading the dermis showing anisocytosis and mitoses (arrow). Haematoxylin and eosin ×400.

Crookes Healthcare Ltd; Nottingham, UK). Fly repellent was applied around the margins of the lesions.

A biopsy from the skin mass was submitted for histological evaluation. The mass showed diffuse change consistent with avascular necrosis, nevertheless where architecture was discernible there were focal areas of exophytic squamous epithelial proliferation contained by a basement membrane. Considering the exophytic growth pattern and general cytological features, the lesion was considered to resemble a cornifying infundibular keratinizing acanthoma. However, given the superficial and necrotic nature of the biopsy, the proliferative epithelial component and the known risk of continued sunlight exposure potentially exacerbating pre-existing squamous proliferative lesions, regular monitoring was advised due to the possibility of underlying SCC.

Approximately 6 months later the rhinoceros was anaesthetized to excise the skin mass because it had increased in size from 1W × 2L cm to 3W × 3L. A combination of butorphanol and azaperone was used based on the chemical restraint regime published by Radcliffe *et al.*[12] It was initially darted with 100 mg azaperone (40 mg mL^{-1} Stresnil™, Janssen Animal Health; Saunderton, UK) combined with 70 mg butorphanol (10 mg mL^{-1} Torbugesic injection™, Forte Dodge Animal Health; Southampton, UK). This was followed 30 min later by a top-up dosage by dart (40 mg azaperone and 30 mg butorphanol) and a final top-up dose 20 min later given intravenously (ear vein). Throughout the surgical procedure further increments were given intravenously to a total of 40 mg azaperone and 30 mg butorphanol. Lactated ringers solution was also given intravenously during surgery and oxygen was supplemented nasally (2 L min^{-1}). Local anaesthetic (Locaine 2%™, Animalcare Ltd; York, UK) was injected around the surgery site. A number 20 scalpel blade was needed to excise the mass. The skin mass was excised with wide margins and submitted for histological evaluation. Two separate skin biopsy was taken at other sites along the flank. Primary skin closure of the tumour incision site was not possible. Stay sutures (Ethilon 3/0, Ethicon™, Johnson-Johnson Intl; St-Stevens-Woluwe, Belgium) were placed at the corners of the wound and a nonadhesive dressing was attached (Allevyn™, Smith and Nephew, Hull, UK). The wound deficit was filled with Intrasite gel™ (Smith and Nephew; Hull, UK). The dressing and gel were replaced every third day for 3 weeks. Fly repellent was applied around the wound and on the bandage. The surgery site had healed completely within a month. Ideally integument should be monitored for lesions every 3 months in the first year including local draining lymph nodes. The animal was monitored visually by the zoo staff until it was euthanized 2 years later for an unrelated condition.

Histopathological examination of the excised skin mass confirmed the presence of a well-differentiated SCC characterized by islands and papillary projections of proliferating squamous epithelium. The epithelium was generally well polarized however, at the base of the lesion, small cohesive nests were evident, infiltrating into the dermal connective tissue. Although generally well differentiated, there was moderate to marked anisocytosis in some areas and occasional bizarre mitoses were also seen (fig. 2). Overall, the mitotic rate was very variable ranging from 0 to 3 per high power field. There was a prominent lymphoplasmacytic inflammatory reaction in many areas surrounding the deep margins of the infiltrating epithelial cells. There appeared to be an adequate excision margin around the mass.

In addition, the two skin biopsies revealed a moderate eosinophilic pustular dermatitis suggestive of a hypersensitivity reaction, possibly to ectoparasites.

Discussion

Squamous carcinoma is a neoplasm of the keratinizing cells that shows malignant characteristics, including anaplasia, rapid growth, local invasion and metastatic potential. Although UV light exposure is commonly sited as a causal factor, genetic mutations, immunosuppression, viral infections, and chronic inflammation have also been implicated in the pathogenesis of SCC.[13] In the domesticated species, they are considered common tumours and have been reported in dogs, cats, horses, cattle, sheep and goats.[14] They are largely considered a disease of local invasion rather than high metastatic potential. However, in most domestic species, this biology is considered to

be site dependent with some tumours, e.g. SCC of the digit in canids, having a greater incidence of metastatic lesions.[15]

It is possible that the chronic irritation and injury potentially caused by birds as noted by the zoo keepers played a part in the initial development of an infundibular keratinizing acanthoma on its flank. In black rhinoceros, *Diceros bicornis*, the skin undergoes marked epidermal hyperplasia in response to injury.[1] It is presumed that age, chronic inflammatory dermatosis and scars as well as exposure to the sun contribute to higher incidence of skin neoplasia. Black rhinoceros skin has features that most closely resemble those of human skin except for deep collagenous dermis.[1]

The few existing reports of skin neoplasia in rhinoceros describe ulcerated wounds located close to the horn.[9,10] Naik *et al.*[9] described a SCC in an Indian rhinoceros, *Rhinoceros unicornis*, in the skin over the nose adjoining the horn. At the time of diagnosis, the tumour was inoperable. Constant trauma to the base of the horn may have contributed to the development of the SCC. A similar case was discussed by Nandi *et al.*,[10] describing a cauliflower growth with ulcerated surface at the base of the horn. Based on our experience this does not always seem to be the case as the tumour was located over the flank. A brief report by Aylmer[11] on a skin carcinoma in a white rhinoceros does not elaborate on the type and location of the skin carcinoma or the outcome of the surgery.

Squamous cell carcinoma in the rhinoceros may be treatable with surgery, provided that complete excision is possible. Although local invasion may be severe, as in reported cases involving the area of the horn, distant metastases have not been reported. In this case, no signs of metastasis were seen 2 years later, when the animal underwent gross post-mortem examination for unrelated chronic arthritis. Wound healing by secondary intention is a feasible option when primary wound closure is not possible.

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Résumé Un rhinocéros blanc, mâle âgé de 33 ans, présentant une dermatite saisonnière, a présenté un carcinome épidermoïde malin du flanc droit. *Staphylococcus aureus* a été cultuvé à partir des lésions cutanées. Aucun dermatophyte ou levure n'a été observé. La dermatite a été traitée par une combinaison d'un antibiotique par voie orale (trimethoprime-sulphadiazine) et par voie topique avec des bains à la chlorhexidine une fois par semaine et une crème à base d'oxyde de zinc, de baume du pérou et d'oxide de bistmuth. La tumeur a été chirurgicalement retirée sous anesthésie à l'azaperone et au butorphanol. La tumeur ayant été enlevée avec de larges marges, une cicatrisation par seconde attention a été réalisée, car il fut impossible de refermer la plaie. A l'autopsie réalisée deux ans plus tard, pour une maladie non en rapport, aucune métastase ou récidive de la tumeur ne fut observée. Il est supposé qu'une irritation chronique ou des traumatismes aient été à l'origine de l'apparition de la tumeur. Il s'agit du premier rapport détaillé de l'efficacité d'un traitement d'un carcinome épidermoïde non localisé à la corne chez le rhinocéros.

Resumen A un rinoceronte blanco en cautividad de 33 años de edad con dermatitis estacional se le diagnosticó carcinoma de células escamosas en el flanco derecho. Se cultivó *Staphylococcus aureus* de las lesiones de la piel. No se aislaron hongos ni levaduras. La dermatitis se trató con una combinación de antibióticos orales (trimetoprim-sulfadiazina) y tópicamente con lavados semanales de clorexidina y una mexcla de óxido de zinc, balsamo de Perú y crema de óxido de bismuto. Bajo anestesia de azaperona y butorfanol se extirpó el tumor quirúrgicamente. El tumor se extirpó con amplios margenes y se permitió la

cicatrización por intención secundaria, ya que no se pudo cerrar la herida primaria. El estudio post-mortem desarrollado dos años más tarde debido a otra condición no desveló presencia de enfermedad metastática ni recidiva del tumor. Presumiblemente irritación crónica o trauma podían haber contribuido al desarrollo del tumor. Este es el primer estudio detallado del tratamiento con éxito de un carcinoma de células escamosas no asociado con el cuerno en un rinoceronte.

Zusammenfassung Ein in Gefangenschaft gehaltenes dreiunddreißig Jahre altes männliches weißes Nashorn mit saisonaler Dermatitis wurde mit einem malignen Plattenepithelkarzinom an der rechten Flanke diagnostiziert. *Staphylococcus aureus* wurde von der Hautveränderung kultiviert, während keine Pilze oder Hefen isoliert wurden. Die Dermatitis wurde mit einer Kombination aus oralen Antibiotika (Trimethoprim-Sulphadiazin), topischen wöchentlichen Chlorhexidinbädern und einer Creme, welche aus einer Mischung von Zinkoxid, Perubalsam und Bismuthoxid bestand, behandelt. Unter Narkose, bestehend aus Azaperon und Butorphanol, wurde der Hauttumor chirurgisch entfernt. Der Tumor wurde mit großem Sicherheitsabstand herausgeschnitten und eine Wundheilung 'per secundam intentionem' erlaubt, da ein Schluss der Wunde primär nicht möglich war. Eine Post-mortem Untersuchung zwei Jahre später, die aus anderen Gründen durchgeführt wurde, zeigte keine Metastasen oder ein Wiederauftreten des Hauttumors. Es wurde vermutet, dass möglicherweise die chronische Irritation oder ein Trauma zur Entstehung des Hauttumors beigetragen haben. Es handelt sich hierbei um einen detaillierten Bericht der erfolgreichen Behandlung eines Plattenepithelkarzinoms, welches nicht mit dem Horn des Nashorns assoziiert wurde.

