MUCOSAL AND CUTANEOUS ULCERATIVE SYNDROME IN BLACK RHINOCEROS (*Diceros bicornis*)

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Oral, nasal, and cutaneous ulcers are prevalent in captive black rhinoceros (3,5,7,11) and are a significant health problem resulting in debility, secondary infections, and anemia. Similar ulcers also have been reported in free-ranging black rhinoceros in Africa (1,2,5,8,9,12) and are associated with *Stephanofilaria dinniki* infestation. However, no parasites have been noted in ulcers of captive rhinos, and the cause has remained elusive. The purpose of this study was to characterize these ulcers histopathologically and to determine the pathogenesis of these lesions with the intention of identifying the etiology.

Twenty-six captive rhinoceros in the United States have had mucosal and/or cutaneous ulcers and most of these rhinos have had multiple recurrences. Both sexes are affected (11 males and 15 females) and their ages ranged from 1.5 to 36 years. Only rhinos between 6-12 years were underrepresented in the affected population. Affected rhinos were housed at 14 zoos in all geographical areas of the United States and 7 of these 14 zoos have had multiple cases.

The clinical presentation for most cases was similar and was characterized by a sudden onset of elevated cutaneous plaques (papules) which progressed rapidly to form vesicles or pustules and then ulcers. Many ulcers extended peripherally and adjacent ulcers often coalesced, resulting in expansive areas of denuded skin affecting up to 70% of the rhinoceros. Ulcers healed poorly, resulting in a prolonged clinical course. Ulcers eventually regressed either spontaneously or in response to corticosteroid and/or antibiotic treatment.

The distribution of cutaneous ulcers was predominantly on pressure points (lateral hocks, stifles, elbows) and at the periphery of appendages (tips of ears, coronary bands, feet, tip of tail). More severe cases had ulcers over most of the ventral and lateral abdomen and chest.

The development of oral and nasal ulcers has not been as well characterized. The clinical sign in most rhinos with nasal lesions was epistaxis, and oral ulcers were noted because of dysphagia or hypersalivation. Mucosal ulcers also expanded peripherally and healed slowly. Most oral ulcers were present on the lips and palate and less frequently on the tongue.

Biopsy or necropsy samples of ulcers were examined histopathologically in 14 cases (11 of these 14 by the author). The principle primary disease process was confined to the epithelium. Acute lesions (grossly characterized as papules) had marked intercellular (spongiosis) and intracellular edema in the epidermis. These lesions progressed to form intraepithelial clefts, vesicles (containing proteinaceous fluid) and/or pustules (containing neutrophils and/or eosinophils). In some cases epithelial cells had ballooning degeneration and rarely dyskeratotic cells. The basal epithelium was normal in most cases, but some areas with hyperplastic or degenerative changes were noted. In all acute and subacute lesions, inflammation in the dermis was minimal or absent. Dermal edema and hemorrhage were present in most cases, and red blood cells extravasated through the epithelium.

Chronic ulcers were covered with a fibrinopurulent crust, had abundant granulation tissue at the ulcer base, and marked acanthosis at the margins. In some cases the epithelial proliferation was pseudocarcinomatous. One nasal ulcer was associated with an invasive

squamous cell carcinoma. The dermis subjacent to chronic ulcers had a marked inflammatory infiltrate composed principally of neutrophils with some eosinophils, monocytes, and plasma cells. In two cases, the eosinophilic infiltrate was intense and associated the collagenolysis and giant cell aggregates (eosinophilic granulomas).

In one case, cells at the junction of the stratum spinosum and stratum corneum had koilocytotic change and nuclei with peripheralized chromatin, suggestive of papovaviral infection. In this and other rhinos, pale pink intracytoplasmic inclusions were noted in epidermal cells, suggestive of poxviral inclusions. However, no virus was noted in either the cytoplasm or nuclei by electron microscopy of one case. The "pox-like" inclusions were composed of clusters of intermediate filaments, compatible with keratin. The keratin content of these inclusions was confirmed with immunocytochemical stains. Viral isolation was attempted on vesicle fluids from two cases and no viruses were identified.

Two cases were examined by immunofluorescence for the presence of autoantibody using anti-porcine (one case) or anti-equine, and anti-rhinoceros (generously provided by Dr. Hugh Chaplin) immunoglobulins, and both cases were negative. Also, no acanthocytes, typical of immune-mediated disease, were observed histopathologically.

No specific pathogens were isolated from bacteriological examination of several cases. Most bacterial isolates were normal skin commensals, some of which resulted in septicemia after the epithelial barrier was broken (1). Fungi cultured from the lesions also were opportunistic.

Many rhinos with ulcers had concurrent systemic diseases. The most prevalent disease associated with the ulcers was anemia (N = 6) which in some, but not all, cases was hemolytic. Other diseases noted were systemic mycosis, hepatic fibrosis, renal disease, and gastrointestinal ulcers. However, some cases that died had no significant lesions other than mucosal/cutaneous ulcers and lymphoid depletion.

The specific cause of these lesions was not apparent from the material available. Autoimmune disease was considered due to the presence of intraepithelial vesicles. However, the high prevalence of the lesions in the captive rhino population, the location of the vesicles in the epithelium (stratum spinosum), the absence of acanthocytes or typical inflammatory infiltrate, as well as the lack of evidence for autoantibody in the lesions, does not support this diagnosis. Intraepithelial vesicles and ballooning degeneration of epithelial cells are features of viral diseases, and the occurrence of multiple simultaneous cases in a zoo supports an infectious etiology. However, no viral inclusions or viral particles were noted, and no virus was isolated in two cases. Furthermore, the persistence and recurrence of the lesions is not typical of known epithelial viral diseases in other species.

Characteristics of the syndrome in rhinos are similar, but not identical, to several diseases of unknown etiology in man and domestic animals (4,6,10). The features of epidermolysis bullosa are most similar to the syndrome in rhinoceros. Epidermolysis bullosa is an degenerative epithelial disease characterized by skin fragility which results in vesicles and ulcers over pressure points. The disease is prevalent in some breeds of domestic dog and is inherited. However, the histopathological features of basal cell degeneration and subbasal vesicles are not features of the syndrome in rhinoceros. Familial acantholysis of calves is an similar inherited disease of calves, but is characterized by intraepithelial vesicles. However, this disease results in an early death (10). Erythema multiforme is a disease of man and domestic animals characterized by intraepithelial edema, necrosis, and vesicle formation. Approximately 50% of the cases of erythema multiforme are associated with other systemic diseases. However, this is a rare disease in other species and is not associated with ulcers, in contrast to the disease in rhinos. Toxic epidermal necrolysis is considered a more severe, very rare form of erythema multiforme.

The lesions in rhinoceros are unlike any known cutaneous disease due to a nutritional deficiency or excess. A contact toxin is possible, but contact allergies are unlikely because of the lack of pruritus.

In summary, mucosal and cutaneous ulcerative syndrome of black rhinoceros is characterized by a sudden appearance of lesions, a prolonged clinical course, frequent recurrence, and a typical distribution (lips, palate, tongue, pressure points, coronary bands, etc.) of lesions (single or multiple papules, which progress rapidly to vesicles, pustules and then non-healing ulcers) with histological characteristics of a primary epithelial disease. The cause of this syndrome has not yet been identified, but studies are in progress to further explore the possibility of viral, inherited, and toxic etiologies.

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