Vesicular and Ulcerative Dermatopathy Resembling Superficial Necrolytic Dermatitis in Captive Black Rhinoceroses (*Diceros bicornis*)

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**Abstract.** The histopathology, clinical presentation, and epidemiology of a cutaneous and oral mucosal disease affecting 40 black rhinoceroses (*Diceros bicornis*) at 21 zoological parks (50% of the captive US population) were investigated. Twenty-seven biopsies were examined from recent lesions, and clinical information was available from 127 episodes. The cutaneous lesions began as plaques that progressed to vesicles, bullae, or ulcers. Lesions waxed and waned in individual cases. Lesions were predominantly bilaterally symmetrical, affecting pressure points, coronary bands, tips of the ears and tail, and along the lateral body wall and dorsum. Oral lesions were first noticed as ulcers and were present on the lateral margins of the tongue, palate, and mucocutaneous junctions of the lips. All recent lesions had similar histopathologic findings of prominent acanthosis, hydropic degeneration of keratinocytes in the stratum spinosum, spongiosis, intraepithelial vesicles, and parakeratosis without dermal inflammation. Chronic lesions were ulcerated. No pathogens were identified by culture or electron microscopy. Most episodes coincided with stress events (transportation, sudden cold temperatures, intraspecific harassment, estrus, advanced pregnancy) or concurrent diseases (toxic hepatopathy, hemolytic anemia, respiratory or urinary tract infections). Affected rhinoceroses usually were lethargic and had weight loss. Affected rhinoceroses also had lower hematocrit, serum albumin, and cholesterol values than captive healthy or wild rhinoceroses. The clinical patterns and histopathologic findings are similar to those of superficial necrolytic dermatitis in dogs and necrolytic migratory erythema in humans. The high prevalence of this skin disease in captive black rhinoceroses under many circumstances suggests that their epidermis is acutely sensitive to any disruption of metabolic homeostasis. We propose that metabolic changes secondary to a stress response from maladaptation or nutritional inadequacy of captive diets may contribute to the development of this disease in rhinoceroses without hepatopathies.

**Key words:** Black rhinoceros; eosinophilic granulomas; hepatocutaneous syndrome; necrolytic migratory erythema; skin; superficial necrolytic dermatitis; ulcerative skin disease.

**Materials and Methods**

**Study population**

Biopsies were obtained from twenty-one black rhinoceroses that acquired skin plaques, vesicles, or acute ulcers from 1989 to 1994. The clinical and pathology records of black rhinoceroses with a history of similar plaques, vesicles, or ulcers during the period from 1972 (first available clinical records) until 1994 in US zoological parks participating in the American Zoo and Aquarium Association (AZA) Black Rhinoceros Species Survival Plan (SSP) also were reviewed. From historical records, an additional 19 rhinoceroses were selected based on having analogous clinical presentations or similar histopathologic findings in biopsies. Combined, the 21 recently biopsied and 19 historic cases resulted in 40 affected rhinoceroses in the study. These 40 rhinoceroses represent approximately 50% of the US captive population.

The affected population included 19 male and 21 female rhinoceroses, ranging from 1 to 39 years of age (1–5 years, \(n = 4\); 6–15 years, \(n = 11\); 16–30 years, \(n = 21\); >30 years,
n = 4), from 21 zoological parks. Of 36 captive-born rhinoceroses, 21 animals were offspring of wild parents and 15 animals were ≥2 generations removed from the wild. Thirty-one affected rhinoceroses were East African subspecies (D. bicornis michaeli), and nine rhinoceroses were southern African subspecies (D. bicornis minor). These numbers reflect the approximate proportion of each subspecies in the captive population.

Clinical information on affected rhinoceroses was obtained from the medical records and the responses to a questionnaire that was sent to veterinarians at AZA Black Rhino SSP participating zoos. The character, topographic location, and month of initial appearance of skin lesions, number of disease events, treatment outcome, clinical course, and concurrent diseases were recorded. To evaluate patterns of clinical disease, the clinical data were grouped by episode; a single episode was defined as the occurrence of new skin lesions or the recurrence of a former lesion at least 1 month after resolution of previous lesions. Treatment outcomes were considered positive if lesions resolved within 14 days. Clinical chemistry and hematology values from blood drawn within 1 week of an episode were included in population statistics. In cases with serial samples within an episode, the first and last samples from each episode were included. Values from affected rhinoceroses were compared with values from healthy captive or wild rhinoceroses, but no statistical analyses were performed because blood analyses were conducted in different laboratories. Appropriately stored serum or plasma samples from affected rhinoceroses during disease episodes were not available for glucagon or amino acid assays.

Diet information was available from 15 zoos that participated in the Black Rhinoceros SSP. Alfalfa hay was the principal dietary component in 12 zoos, and four zoos fed primarily mixed timothy hay. Two zoos offered browse, including different types of Acacia spp. and Ficus spp. Supplementation with grain and premixed concentrates varied widely among zoos and within the same zoo over time and consisted of hoofstock or herbivore pellets (eight zoos) or horse chow (five zoos). Other grains, bread, fresh vegetables, and fruit supplemented the hay diets at some zoos. Mineral salt supplements also were offered in 12 zoos.

Biopsies

Twenty-seven skin biopsy samples from 21 rhinoceroses were available for histopathology, and biopsies from eight of these rhinoceroses were examined ultrastructurally. Skin or oral mucosal biopsies were derived from the margins of acute and chronic lesions. Full thickness wedge skin samples were fixed in 10% buffered formalin or 4% glutaraldehyde in 0.1 M sodium cacodylate at pH 7.4. For histopathology, the tissues were embedded in paraffin, sectioned at 7 μm, and stained with hematoxylin and eosin (HE). For electron microscopy, glutaraldehyde-fixed sections were embedded in paraffin, sectioned, and stained with HE to identify the specific areas of affected epithelium by light microscopy. The lesion site then was excised from the paraffin block, deparaffinized, postfixed in 2% OsO₄, embedded in Epon, sectioned at 50 nm, stained with lead citrate and uranyl acetate, and examined on a Phillips 301 electron microscope.

Immunohistochemistry

Nine biopsy samples that had cytoplasmic inclusions in keratinocytes were stained for cytokeratins. The 7-μm sections were deparaffinized, dehydrated through graded alcohols, incubated with 0.3% hydrogen peroxide in methanol for 10 minutes to block endogenous peroxides, and washed in phosphate-buffered saline. Tissues then were preincubated in 1% normal goat serum to block nonspecific immunoglobulin binding and incubated in prediluted mouse anti-pancytokeratins (Biogenex Laboratories, San Ramon, CA) for 30 minutes at room temperature. Antibody binding was visualized with anti-mouse immunoglobulin–streptavidin–biotin–peroxidase (Biogenex Laboratories) according to manufacturer’s directions and with diaminobenzidine as a chromogen.

One biopsy of an epidermal vesicle was examined by indirect immunofluorescence for the presence of autoantibody using anti-rhinoceros IgG and whole serum (provided by H. Chaplin, Washington University School of Medicine, St. Louis, MO) and anti-horse IgG and IgM. Another biopsy was examined for autoantibody using anti-porcine IgG, and binding was visualized by fluoresceinated protein G.

Microbial cultures

Primary cell lines of black rhinoceros dermal fibroblasts (provided by O. Ryder) and white rhinoceroses (Ceratotherium simum) dermal fibroblasts and kidney cell lines (provided by L. Munson) were used for virus isolation. Skin samples or vesicle fluid contents from four recently affected rhinoceroses were shipped on dry ice, minced, and applied to subconfluent cell monolayers. Cells were passaged four times and examined for cytopathic effects, and the final passage was negatively stained with 3% phosphotungstic acid and examined on a Phillips electron microscope for virus particles. Standard aerobic bacterial cultures were performed from cutaneous lesions of 11 rhinoceroses.

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Fig. 1. Skin; black rhinoceros. Gross appearance of the vesicular stage of superficial necrolytic dermatopathy and more chronic expanding ulcerative lesions on the hips, stifles, and hocks.

Fig. 2. Skin; black rhinoceros. Closer view of ruptured and intact epidermal vesicles from Fig. 1.

Fig. 3. Skin; black rhinoceros. Gross appearance of the chronic ulcerative stage of superficial necrolytic dermatopathy bilaterally on the stifles, hocks, and coronary bands.

Fig. 4. Skin, coronary band; black rhinoceros. Closer view of chronic ulcerative and proliferative lesions of superficial necrolytic dermatopathy.
Fig. 5. Skin; black rhinoceros. The exfoliative form of superficial necrolytic dermatopathy in which large sheets of superficial epidermis are sloughed.

Fig. 6. Tongue; black rhinoceros. With the oral pattern of superficial necrolytic dermatitis, the ulcers are located along the lateral margins of the tongue in contact with the teeth and on the prehensile portion of the lips (not shown).
Table 1. Most significant lesions in 23 black rhinoceroses that died with concurrent superficial necrolytic dermatopathy.

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>No. Rhinoceroses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary or systemic mycosis</td>
<td>6</td>
</tr>
<tr>
<td>Toxic hepatopathy</td>
<td>5</td>
</tr>
<tr>
<td>Chronic or acute hemolytic anemia</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>2</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>1</td>
</tr>
<tr>
<td>Bacterial pneumonia</td>
<td>1</td>
</tr>
<tr>
<td>Hepatic hemangiosarcoma</td>
<td>1</td>
</tr>
<tr>
<td>Leukoencephalomalacia</td>
<td>1</td>
</tr>
<tr>
<td>Anemia from uterine adenocarcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Salmonellosis</td>
<td>1</td>
</tr>
<tr>
<td>Euthanized due to chronic dermatopathy</td>
<td>1</td>
</tr>
</tbody>
</table>

Results

Clinical findings

One hundred twenty-seven episodes of epidermal disease were noted in the 40 rhinoceroses during the study period. Cutaneous lesions evolved through characteristic stages, beginning as raised plaques that progressed to erosions or ulcers (Figs. 1-4). Many, but not all, cases had an intermediate vesicular or bullous stage. In some rhinoceroses, erosions or ulcers were the first clinical sign noted. Some cases had extensive regional superficial epidermal exfoliation (Fig. 5), and a few rhinoceroses had small transient subcorneal pustules. Chronic ulcers expanded peripherally and developed thick rounded edges, described as vegetative or wartlike. The evolution of lesions in the oral and nasal cavities was not observable. However, ulcers present at these sites (Fig. 6) had raised edges that became protuberant, fungate, and/or hemorrhagic in chronic cases.

Clinical episodes were characterized by sudden onset, followed by spontaneous remission and exacerbation of lesions. Most cases had a prolonged clinical course with eruption over time of lesions at multiple sites and slow reepithelialization of ulcers. Seventeen of the 40 rhinoceroses had recurring episodes (2-22 episodes/rhinoceroses; eight of the 17 rhinoceroses had more than seven episodes), and 23 rhinoceroses had a single episode (from 3 days to several months in duration). Thirteen of these 23 rhinoceroses had unresolved lesions at death, and 10 other rhinoceroses died during an episode (Table 1). Two rhinoceroses with the most persistently recurring disease (13 and 22 episodes) had predominantly oral lesions.

Epidermal lesions were located at pressure points (51 episodes), along the back (18 episodes), and on the coronary bands or feet (17 episodes), lateral body (15 episodes), tail (13 episodes), head (seven episodes), ears (eight episodes), and vulva/prepuce (four episodes) (Fig. 7). Lesions at the pressure points and on the ears and feet typically were bilaterally symmetrical in distribution. Twenty-two episodes involved lesions on the lips, and 55 episodes involved the oral cavity. Oral cavity lesions, when visible, were located on the tongue (particularly at the lateral margins; Fig. 6), hard palate, gingiva, and/or buccal mucosa. Lesions were noted in the nasal cavities or nostrils during seven episodes, and five other episodes involved epistaxis without visual identification of a lesion. One rhinoceros had nasal lesions only, whereas all other rhinoceroses with nasal lesions also had lesions at other sites.

Histopathologic findings

In recently developed lesions and at the margins of chronic ulcerated lesions, the pathologic changes were limited to the epidermis or oral mucosa and were comparable in all affected rhinoceroses. The epithelium had marked hyperplasia with deep, branching, and anastomosing rete pegs (Figs. 8, 9) in comparison with normal rhinoceros skin (Fig. 10). The superficial stratum spinosum had laminar spongiosis and moderate to severe hydropic degeneration of keratinocytes. There was hypogranulosis and regional to diffuse parakeratosis. In cases with severe spongiosis, intraepithelial clefts, vesicles, or bullae formed, many of which contained proteinaceous fluid. The epithelium overlying these vesicles was necrotic and in many cases had exfoliated, resulting in erosions and sometimes ulcers. Most intraepithelial vesicles were acellular or contained a few polymorphonuclear leukocytes. No intravascular acanthocytes were noted. Also, no autoantibodies were identified by indirect immunofluorescence in the two cases examined.

Additional epidermal and mucosal changes noted in some newly developed lesions were disorganization of the stratum spinosum, dyskeratosis, and rarely indistinct eosinophilic cytoplasmic inclusions in keratinocytes. Individual rhinoceroses sometimes also had prominent superficial crusts consisting of cornified...
cells, fibrin, neutrophils, eosinophils, and bacterial colonies or had prominent subcorneal pustules. Biopsies from rhinoceroses with extensive clinical exfoliation were composed of sheets of parakeratotic superficial epithelium.

Pathologic changes in the dermis were minimal or absent in newly developed lesions; the most common findings were edema and hemorrhage, telangiectasia, and neovascularization in the dermal papillae. Inflammatory changes were notably minimal except in the dermis subjacent to ulcers.

Chronic lesions had more extensive ulcers with deep beds of mature granulation tissue in the subjacent dermis or submucosa, but the changes of acanthosis, spongiosis, hydropic degeneration, and parakeratosis were always present at the ulcer margins. In seven cases, chronic ulcers had marked eosinophilic infiltrates and collagen degeneration with mineralization in the adjacent dermis, and four rhinoceroses had eosinophilic granulomas in the deep dermis and subcutis subjacent to their ulcers.

Ultrastructural changes in the epidermis of recently developed lesions were nonspecific. Keratinocytes from the superficial stratum spinosum had mild to marked hydropic degeneration, disorganization and aggregation of microtubules and microfilaments, and intercellular edema (Fig. 11). Keratinocytes in areas of severe spongiosis and overlying the intraepithelial vesicles were necrotic. Some keratinocytes had small irregular clusters of keratin filaments. The larger eosinophilic cytoplasmic inclusions noted in keratinocytes by light microscopy had ultrastructural characteristics of intermediate filament aggregates and were confirmed by immunohistochemistry to be cytokeratins.

**Microbiologic findings**

All viral cultures were negative for cytopathic effects, and no viral particles were identified in either cell cultures or degenerate keratinocytes by electron microscopy. Aerobic bacteria isolated from lesions included *Staphylococcus* spp. (five rhinoceroses), *Streptococcus* spp. (five rhinoceroses), *Escherichia coli* (three rhinoceroses), and *Pseudomonas aeruginosa, Enterobacter cloacae, Aeromonas hydrophila, Peptostreptococcus* sp., and *Bacillus* sp. from single episodes. *Cephalosporium* sp. was cultured from one lesion, but no fungi were identified in the lesions by light microscopy.

**Clinical pathology**

Serum chemistry, electrolytes, and hematology values for affected rhinoceroses are compared with values for unaffected captive and wild black rhinoceroses in Tables 2 and 3. Affected rhinoceroses had lower hematocrit, serum albumin, and cholesterol values and lower calcium concentrations than did healthy captive or wild rhinoceroses. Affected rhinoceroses had higher white blood cell counts and higher chloride, serum urea nitrogen, globulin, total bilirubin, gamma glutamyl transpeptidase (GGT), and aspartate aminotransferase (AST) values than did healthy captive or wild rhinoceroses and higher lactate dehydrogenase (LDH)
Fig. 9. Skin; black rhinoceros. Chronic recurrent lesions were present during sudden cold temperatures (primary disease). The epidermal changes of lesions arising without hepatopathy are similar to those in Fig. 8, although they are more severe and chronic. HE. Bar = 100 μm.

Fig. 10. Skin; black rhinoceros. This animal had no current or previous skin disease. HE. Bar = 100 μm.

and alanine aminotransferase than did healthy captive rhinoceroses. When toxic hepatopathy cases were excluded from analyses, only LDH, GGT, and AST were higher than mean values for healthy captive rhinoceroses, but all were within ranges considered normal for captive rhinoceroses. Five affected rhinoceroses had serum phosphorus levels of <3.0 mg/dl during one or more episodes, but these rhinoceroses also had serum phosphorus levels within the reference ranges during other episodes. The mean level of serum phosphorus for the population of affected rhinoceroses was slightly below values for unaffected captives, but higher than values for healthy free-ranging rhinoceroses.

Concurrent diseases or events

Twenty-three of the 34 rhinoceroses with detailed clinical histories had systemic disease or other notable clinical conditions coincident with the appearance of the epidermal or oral lesions. Concurrent diseases included anemia (17 rhinoceroses), gastrointestinal diseases (14 rhinoceroses, including seven rhinoceroses with gastrointestinal ulcers), liver disease (eight rhinoceroses, including five rhinoceroses with severe toxic hepatopathy), respiratory tract infections (eight rhinoceroses, including five rhinoceroses with mycotic pneumonia), and urinary tract diseases (six rhinoceroses). The most significant lesion of the 23 rhinoceroses that died or were euthanatized during an episode are outlined in Table 1. Also reported were notable weight loss (12 rhinoceroses), unexplained lameness (12 rhinoceroses), depressed attitude (11 rhinoceroses), anorexia (seven rhinoceroses), and weakness (three rhinoceroses). Eight rhinoceroses were pregnant at the time of lesion development, and disease episodes also occurred concurrently with estrus or breeding in two other rhinoceroses. Six rhinoceroses developed cutaneous disease immediately after transportation or introduction of a new rhinoceros into the enclosure, which resulted in intraspecies aggression.

Geographic distribution and seasonality

Affected rhinoceroses were housed at 21 zoological parks distributed through all geographic regions of the USA that house rhinoceroses (Fig. 12). Twelve zoos had multiple cases, and nine zoos with multiple rhinoceroses had only one rhinoceros affected. Disease episodes occurred throughout the year, with a trend toward more cases during cold months (40% of the
Fig. 11. Transmission electron micrograph. Skin, superficial stratum spinosum; black rhinoceros. The keratinocytes have hydropic degeneration, no keratohyalin granules, and intercellular edema. Lead citrate and uranyl acetate. Bar = 5 μm.

Table 2. Serum chemistry values for captive black rhinoceroses with vesicular and ulcerative dermatopathy (SND), healthy captive rhinoceroses, and healthy wild rhinoceroses.

<table>
<thead>
<tr>
<th>Serum Component</th>
<th>SND</th>
<th>Healthy Captive</th>
<th>Healthy Wild</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\bar{x}$ ± SD</td>
<td>$\bar{x}$ ± SD</td>
<td>$\bar{x}$ ± SD</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>86.8 ± 34.8</td>
<td>80 ± 29</td>
<td>97.3 ± 49.23</td>
</tr>
<tr>
<td>Sodium (mEq/liter)</td>
<td>130.2 ± 8.6</td>
<td>131 ± 3</td>
<td>133.5 ± 6.6</td>
</tr>
<tr>
<td>Potassium (mEq/liter)</td>
<td>4.8 ± 1.2</td>
<td>4.6 ± 0.5</td>
<td>4.39 ± 0.5</td>
</tr>
<tr>
<td>Chloride (mEq/liter)</td>
<td>98.1 ± 7.8</td>
<td>96 ± 3</td>
<td>94 ± 4.5</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>11.1 ± 1.1</td>
<td>12.4 ± 0.08</td>
<td>11.5 ± 1.1</td>
</tr>
<tr>
<td>Phosphorus (mg/dl)</td>
<td>4.06 ± 1.5</td>
<td>4.5 ± 1.2</td>
<td>3.7 ± 1</td>
</tr>
<tr>
<td>Urea nitrogen (mg/dl)</td>
<td>15.5 ± 6.3</td>
<td>13 ± 3</td>
<td>9.9 ± 2.2</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.10 ± 0.28</td>
<td>1.2 ± 0.2</td>
<td>1.17 ± 0.3</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>0.45 ± 0.27</td>
<td>0.6 ± 0.3</td>
<td>3.6 ± 0.4</td>
</tr>
<tr>
<td>Total protein (g/dl)</td>
<td>8.38 ± 1.5</td>
<td>7.9 ± 1</td>
<td>8.4 ± 0.6</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>2.16 ± 0.5</td>
<td>2.7 ± 0.3</td>
<td>3.6 ± 0.4</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>6.67 ± 1.2</td>
<td>5.2 ± 0.6</td>
<td>4.6 ± 0.5</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>73.8 ± 24.6</td>
<td>96 ± 41</td>
<td>90 ± 22.9</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>1.77 ± 3.8</td>
<td>0.30 ± 0.2</td>
<td>0.43 ± 0.2</td>
</tr>
<tr>
<td>Lactate dehydrogenase (IU/liter)</td>
<td>847.8 ± 969.2</td>
<td>364 ± 152</td>
<td>1097 ± 371.5</td>
</tr>
<tr>
<td>$\gamma$ glutamyl transpeptidase (IU/liter)</td>
<td>50.8 ± 45.6</td>
<td>32 ± 20</td>
<td>19.4 ± 3.8</td>
</tr>
<tr>
<td>Alanine aminotransferase (IU/liter)</td>
<td>21.0 ± 18.1</td>
<td>13 ± 7</td>
<td>24 ± 8.5</td>
</tr>
<tr>
<td>Aspartate aminotransferase (IU/liter)</td>
<td>137.1 ± 94.9</td>
<td>80 ± 37</td>
<td>82 ± 23.5</td>
</tr>
<tr>
<td>Alkaline phosphatase (IU/liter)</td>
<td>117.2 ± 168.8</td>
<td>106 ± 174</td>
<td>217 ± 251.4</td>
</tr>
</tbody>
</table>

* $n$ = number of rhinoceroses.
† nd = not determined.
Table 3. Hematologic values for captive black rhinoceroses with vesicular and ulcerative dermatopathy, healthy captive rhinoceroses,22 and healthy wild rhinoceroses.28

<table>
<thead>
<tr>
<th>Hematologic Measurement</th>
<th>SND</th>
<th>Healthy Captive</th>
<th>Healthy Wild</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count ( \times 10^3 )</td>
<td>12.22 ± 7.27</td>
<td>9.84 ± 3.1</td>
<td>11.5 ± 4.1</td>
</tr>
<tr>
<td>Red blood cell count ( \times 10^6 )</td>
<td>4.79 ± 3.8</td>
<td>4.17 ± 1.1</td>
<td>5.26 ± 0.6</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.16 ± 5.04</td>
<td>12.6 ± 2.8</td>
<td>16.1 ± 1.8</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>33.32 ± 13.7</td>
<td>35.7 ± 7.8</td>
<td>43 ± 5.1</td>
</tr>
<tr>
<td>Mean corpuscular volume (fl)</td>
<td>91.9 ± 11</td>
<td>87.1 ± 10.6</td>
<td>82.5 ± 7.2</td>
</tr>
<tr>
<td>Mean corpuscular hemoglobin (pg)</td>
<td>32.38 ± 3.2</td>
<td>30.8 ± 3.4</td>
<td>30.9 ± 2.3</td>
</tr>
<tr>
<td>Mean corpuscular hemoglobin concentration (%)</td>
<td>35.57 ± 1.5</td>
<td>35.5 ± 1.7</td>
<td>37.7 ± 4</td>
</tr>
</tbody>
</table>

\( n = \) number of rhinoceroses.

Response to treatment

Treatments included topical antimicrobials (23 rhinoceroses), systemic antibiotics (15 rhinoceroses), and systemic corticosteroids (seven rhinoceroses), as well as hydrotherapy, moisturizing salves, and topical vitamins. Clinical improvement was variable regardless of treatment, and many lesions resolved without treatment.

Discussion

The epidermal disease in all rhinoceroses in this study had a similar clinical presentation with 1) a sudden onset of plaques that progressed to an intermediate stage of vesicles or bullae or directly to ulcers, 2) exacerbations and spontaneous remissions of lesions, and 3) a bilaterally symmetrical distribution of lesions at pressure points and peripheral locations of the body. Cutaneous and oral lesions in all biopsied rhinoceroses had similar histopathologic changes of acanthosis, laminar hydropic degeneration of epithelial cells and spongiosis in the stratum spinosum, hypogranulosis, parakeratosis, and no inflammatory response. This clinical presentation and these pathologic findings are distinctive characteristics of superficial necrolytic dermatitis (SND) in dogs1517,25,39,47 and necrolytic migratory erythema (NME) in humans.1,2,4,54,51 However, the high prevalence of this disease in the captive black rhinoceros population is not typical of either NME or SND. The widespread occurrence of SND in black rhinoceroses may indicate that this disease represents an epidermal sensitivity to a variety of metabolic changes that initiate structural and functional modifications resulting in increased skin fragility.

In dogs or humans, the metabolic disorders that result in SND or NME are associated with factors that cause abnormal glucose metabolism and hypoaminoacidemia. In dogs, cases of SND have been associated with functional pancreatic islet \( \alpha \)-cell neoplasms (glucagonomas),16 diabetes,57 liver disease,39 or poor diets.4-6 In humans, NME occurs almost exclusively with hyperglucagonemia from a functional glucagonoma, although identical skin lesions have been reported recently in humans with liver disease, pancreatic insufficiency, gluten-sensitive enteropathy, and nutritional deficiencies, such as vitamin B12 deficiency and kwashiorkor.33,37,51,54,55 High glucagon levels cause this lesion by inducing hypoaminoacidemia through prolonged gluconeogenesis that depletes serum amino acids.1,34,51 No rhinoceroses with SND that were necropsied had glucagonomas nor is the high prevalence of this disease in the captive rhinoceros population (50% of US population) consistent with a neoplastic source of glucagon. Unfortunately, we were unable to determine if glucagon or amino acid levels were abnormal because properly handled sera were not available from affected animals.21

SND has been noted in dogs with liver disease (hepatocutaneous syndrome),17,39 and five rhinoceroses in our study and one other rhinoceros22 had severe toxic
hepatopathy from creosote exposure. Some rhinoceroses (N. Kock, personal communication). Black rhinoceroses differ markedly in their response to SND in other species except humans. Neither zinc nor biotin deficiencies cause the hydropic degeneration of keratinocytes and spongiosis that were noted in the black rhinoceroses, except in humans with acrodermatitis enteropathica (familial zinc malabsorption) or vitamin B₃ deficiency. Considering the morphologic similarities between rhinoceros and human skin, these potential deficiencies should be further explored.
Differences between our findings and the previous reports of skin disease in captive black rhinoceroses can be explained by the chronicity of the lesions in those reports. The acute degenerative changes we noted in the epidermis rapidly progress to reported chronic ulcerative dermatitis and eosinophilic granulomas. Early bullous lesions were not examined in these cases. Although pox virus was identified with chronic ulcerative dermatitis and eosinophilic granulomas, no specific etiologic agents were noted in our cases nor in any previous cases in the United States. The cytoplasmic inclusions noted in keratinocytes of some captive US rhinoceroses were confirmed to be keratinocyte maturation. Also, no specific bacterial pathogens were noted in our cases, although Streptococcus group L and Staphylococcus aureus were thought to be significant isolates from ulcers in previous reports.

The skin lesions in black rhinoceroses from US zoos also differed in distribution, character, and seasonal occurrence from Stephanofilaria-induced lesions noted in wild black rhinoceroses. Lesions in African rhinoceroses were predominantly on the ventral neck, forelegs, and shoulders, were highly pruritic, and occurred in summer months. In contrast, lesions on captive black rhinoceroses occurred year-round, were non-pruritic, and were predominantly at pressure points, in the oral cavity, and on distal extremities (feet, ears, tail). Lesions on African rhinoceroses also are notably inflammatory and associated with filarial larvae and adults, whereas lesions in captive rhinoceroses lack parasites and inflammatory changes.

In summary, black rhinoceroses in zoological parks appear uniquely predisposed to a skin disease resembling superficial necrotic dermatitis in dogs and necrolytic migratory erythema in humans. The high prevalence of SND in this population indicates that diseases with these clinical and histologic characteristics can arise in conjunction with a variety of metabolic disorders. Although no common underlying metabolic disease was specifically identified, stress- or disease-induced hypoaminoacidemia in concert with possibly inappropriate captive diets are suspected as the basis for the high prevalence of these skin problems in captive black rhinoceroses. Future investigations will include in depth diet analysis of captive and wild rhinoceroses, plasma amino acid and essential fatty acid profiles of affected and wild black rhinoceroses, and measurement of plasma glucagon.

Acknowledgements

We thank Dr. Ed Dubovi and Dr. Melissa Kennedy for viral cultures, Teena Smith and Dr. P. J. Felsburg for immunofluorescent techniques, Drs. Mike Burton, Doug Pernikoff, and Mark Campbell for gross photographs, Kreis Weigle and Phil Snow for computer imaging assistance, and Debbie Haines for the rhinoceros drawing. We also thank the following zoos and their veterinarians for contributing materials for this study: Zoo Atlanta (Dr. Rita McManamon), Brookfield Zoo (Dr. Lyndsay Phillips), Busch Gardens of Tampa (Dr. John Olsen), Caldwell Zoo (Dr. Doyle Starnes), Columbus Zoo (Dr. Ray Wack), Cincinnati Zoo (Dr. Mark Campbell), Dallas Zoo and Gladys Porter Zoo (Dr. Tom Alvarado), Denver Zoo (Drs. Richard Cumbre and David Kenney), Detroit Zoo (Dr. Robyn Barbiers), Fossil Rim and Benson Ranches (Dr. Evan Bliemer), Lincoln Park Zoo (Dr. Tom Meehan), Los Angeles Zoo (Dr. Ben Gonzales), Miami Metrozoo (Drs. Chris Miller and Scott Citino), Oklahoma City Zoo (Dr. Mike Barrie), Saint Louis Zoo (Dr. EricMiller), San Diego Zoo and Wild Animal Park (Dr. Don Janssen), San Francisco Zoo (Dr. Avery Bennett), Sedgwick Park Zoo (Dr. Othello Curry), and White Oak Conservation Center (Dr. Janet Stover). This project was funded with support from the University of Tennessee.

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