COMPARATIVE PATHOLOGY OF IRON-STORAGE DISORDERS IN CAPTIVE RHINOCEROSES: POTENTIAL INSIGHTS INTO ETIOLOGY AND PATHOGENESIS

Donald E. Paglia, MD

UCLA Hematology Research Laboratory, Department of Pathology & Laboratory Medicine, UCLA School of Medicine, 10833 LeConte Ave., Los Angeles CA 90095-1732 USA

Abstract

Browser rhinoceroses, (African black [*Diceros bicornis*] and Sumatran [*Dicerorhinus sumatrensis*]),[7,10] along with tapirs (*Tapirus* spp.)[8] and many other endangered wildlife,[6] develop pathologic overloads of iron as a function of time in captivity; whereas grazer rhinoceroses, (African white [*Ceratotherium simum*] and Asian greater one-horned [*Rhinoceros unicornis*]), do not.[7,10] Recent contributions by others[1-5] in deciphering the complex control mechanisms involved in iron homeostasis now allow plausible hypotheses regarding the genetic basis for such differences. An antimicrobial peptide, hepcidin, has recently been identified as the principal hormonal regulator of mammalian iron balance by its interaction with ferroportin, the sole transmembrane channel for egress of cellular iron into plasma. Hepcidin deficiencies are responsible for most forms of hereditary iron overload syndromes in humans, and overproduction of hepcidin induces the anemia of inflammation or chronic disease, another condition commonly observed among captive rhinoceroses.

Histopathologic observations of necropsy tissues from approximately sixty captive rhinoceroses of these four species revealed patterns of iron-pigment deposition that differed from those seen in classical HLA-linked hereditary hemochromatosis or those associated with hemolytic or other anemic conditions. Instead, deposition of iron pigments heavily affected the reticuloendothelial system before involving hepatic and other parenchymal cells in distribution patterns that conformed most precisely to those observed in African (Bantu) iron overload syndrome,[9] a condition characterized by both increased bioavailability of dietary iron and a genetic propensity for its increased assimilation.

These observations support an hypothesis that genetic mutations or polymorphisms resulting in defective hepcidin, ferroportin, or their interaction, could account for the uniform tendency of browser, but not grazer, rhinoceroses (among other wildlife species) to rapidly develop pathologic iron overburdens in captivity. Based on comparative pathology and blood and tissue assays, this difference between rhinoceros species could most likely be explained by an impaired response of ferroportin to modulation by hepcidin in the browsers. Collaborative studies have been initiated to test this hypothesis by sequencing the genes governing expression of hepcidin, ferroportin, and three other key proteins involved in orchestration of iron homeostasis in all four available species of rhinoceroses.

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