

PHEOCHROMOCYTOMA IN A WHITE RHINOCEROS (*CERATOTHERIUM SIMUM*)

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Abstract: A 46-yr-old male white rhinoceros (*Ceratotherium simum*) died during anesthesia following agonal excitation. On postmortem, a well-demarcated 2.5-cm tan mass was identified in the right adrenal gland. Histopathology confirmed the presence of a pheochromocytoma, and elevated levels of epinephrine in serum collected shortly prior to the animal's death, as compared with sera from healthy controls, demonstrated the functional nature of the tumor. Although rare, pheochromocytoma should be considered as a differential diagnosis in cases of suspected hypertension and acute death in rhinos.

Key words: Pheochromocytoma, white rhinoceros, *Ceratotherium simum*, neoplasia, epinephrine, norepinephrine.

BRIEF COMMUNICATION

A 46-yr-old male white rhinoceros (*Ceratotherium simum*) with no significant medical history was sedated for attempted electroejaculation with etorphine (Pharmaxim, 253 68 Helsingborg, Sweden, 0.6 µg/kg) and detomidine (Orion, 02200 Espoo, Finland, 9 µg/kg). During anesthetic induction the rhino was very stiff, showed labored puffing respiration, and developed a staring glance. After approximately 20 min, he became recumbent; electrical stimulation was applied rectally, and the animal went into cardiac arrest.

A complete necropsy (excluding brain) was commenced approximately 1 hr after death. Macroscopic findings included osteoarthritis of both stifles and spondylosis of the cranial thoracic and lumbar vertebrae. Furthermore, there was marked dental calculus, testicular atrophy, polycystic kidneys, pulmonary congestion, and occasional epicardial petechiae. In the right adrenal gland, a 2.5-cm spherical tan mass extended from the medulla, compressing the adjacent cortical tissue (Fig. 1a). Histologically, the adrenal mass was well demarcated and comprised relatively well-differentiated large round to polyhedral cells containing large open-faced nuclei with large nucleoli and well-staining granular basophilic

cytoplasm (Fig. 1b). Peripherally, the cells were mostly arranged in rows, whereas centrally there was an acinar to nested pattern. The mass was well vascularized. Using immunohistochemistry (Fig. 1c), the cytoplasmic granules were found to be chromogranin A-positive.¹⁰

In the lung, there was marked anthracosis and acute congestion, both interpreted as incidental findings. Several vessels showed reversible hypertensive changes consisting of arteriolar sclerosis and medial hyperplasia. Similarly, multiple renal arteries and arterioles showed mild to moderate intimal proliferation interpreted as arterio- and arteriosclerosis.

A serum sample obtained minutes prior to the animal's death was stored at –70°C for 12 mo and then analyzed for catecholamines using standard high-performance liquid chromatography methods with electrochemical detection after alumina extraction of the serum samples¹³ at the Department of Biology, University of Ottawa, Canada. Serum samples from four clinically healthy anesthetized, but not electroejaculated, white rhinos, stored similarly for 6 mo to 2 yr were analyzed at the same time for comparison. Results of a complete blood count and serum biochemical analysis were within reference range for this species.⁶ Compared with values from four clinically healthy white rhinos, the levels of epinephrine and norepinephrine in the animal in question were elevated 16-fold and fivefold, respectively (Table 1).

Discussion

Pheochromocytomas are tumors of the chromaffin cells in the adrenal medulla. They occur rarely in domestic species and have been diagnosed sporadically in exotic species including a

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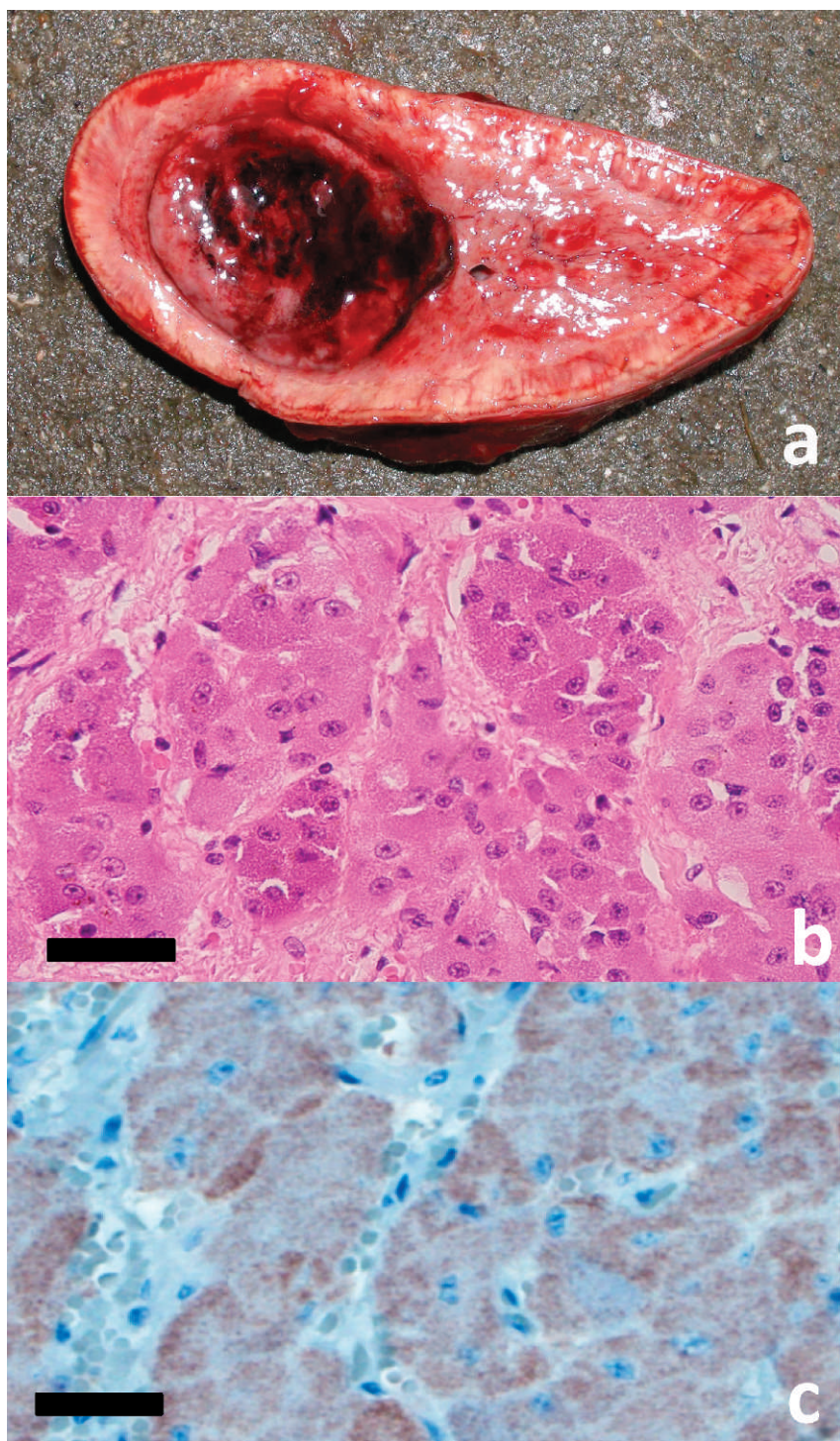


Figure 1. a. Gross image of the right adrenal gland of a 46-yr-old rhinoceros. b. Micrograph showing large uniform cells with basophilic cytoplasm (hematoxylin and eosin). Bar = 150 μ m. c. Micrograph showing granular staining (brown) with chromogranin A. Bar = 150 μ m.

Table 1. Serum values of epinephrine and norepinephrine in a white rhinoceros with pheochromocytoma, compared to four normal controls.

	Normal rhinos (<i>n</i> = 4)		Affected rhino
	Mean $\pm$ SD	Range	
Epinephrine (nmol/L)	2.08 $\pm$ 0.5	1.44–2.75	34.28
Norepinephrine (nmol/L)	11.11 $\pm$ 5.7	5.06–18.48	59.60

sea otter (*Enhydra lutris*),¹² a ring-tailed lemur (*Lemur catta*),⁹ a hippopotamus (*Hippopotamus amphibius*),⁴ an African elephant (*Loxodonta africana*),¹ and a warthog (*Phacochoerus aethiopicus*).³ A familial form has been reported in Asian raccoon dogs (*Nyctereutes procyonides*).¹¹

Diagnosis relies on typical histologic appearance combined with immunohistochemical staining for chromogranin A^{7,10} or with electron microscopy.¹ Functional pheochromocytomas produce catecholamines, typically either primarily epinephrine or norepinephrine. In this case, serum epinephrine and norepinephrine levels were elevated 16-fold and fivefold, respectively. The effects of these substances ultimately lead to the demise of the host, typically through continued or intermittent hypertension. One of the side effects of potent opioids, as well as detomidine, is an increase in blood pressure,^{5,14} and while widely used, etorphine is known to induce hypertension.^{2,8} In the case at hand, a high blood pressure combined with the hypertensive effects of the anesthetic drugs and the stress of the anesthetic event likely led to hypertensive collapse. It may be further speculated that a sudden surge in catecholamines induced by the electrical stimulation for electroejaculation could have added to this cascade.

Antemortem diagnosis of pheochromocytoma is challenging due to the vague clinical signs such as weakness, lethargy, weight loss, and tachypnea. However, serum and urine catecholamine determination would be a diagnostic option available to most clinicians, and pheochromocytoma should be considered as a differential diagnosis in cases of suspected hypertension and acute death in rhinos.

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