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Case Series

Spontaneous Pituitary Neoplasm in Two Female Geriatric Southern Giant Pouched Rats (*Cricetomys ansorgei*)

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Southern giant pouched rats (*Cricetomys ansorgei*) are a small muroid species native to the sub-Saharan Africa. Their exceptionally developed olfactory system, trainability, and relatively small size makes them useful working animals for various applications in humanitarian work. At our institution, a breeding colony of Southern giant pouched rats is maintained to study their physiology and utility as scent detectors. This case report describes the occurrence of spontaneous pituitary neoplasms with distinct clinical presentations in 2 geriatric (approximately 7.5 y old) wild-caught female Southern giant pouched rats. The first pouched rat displayed vestibular deficits, including left-sided head tilt, ataxia, disorientation, and circling. MRI revealed a large, focal heterogeneous mass arising from the pituitary fossa. The second pouched rat presented with polyuria, polydipsia, and hyperglycemia but no neurologic signs. Examination after euthanasia revealed a prolactin (PRL)-expressing pituitary carcinoma and adenoma in the first and second pouched rat, respectively, associated with mammary hyperplasia in both animals. This is the first report of spontaneous PRL-producing pituitary tumors in Southern giant pouched rats.

Abbreviations and acronyms: PRL, prolactin; TSH, thyroid-stimulating hormone

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Introduction

Cricetomys spp. (African giant pouched rats) are nocturnal rodents native to the African savannah in the family of *Nesomyidae.* Nesomyid rodents, such as African giant pouched rats, are distantly related to rodents of the *Muridae* family, such as mice and rats.[9,27] African giant pouched rats (pouched rats) are named based on their characteristic cheek pouches, used for food foraging, and their large size as compared with other rodent species. The genus *Cricetomys* encompasses several species, including *C. ansorgei* (Southern giant pouched rat, subject of this report), *C. gambianus*, *C. emini*, and *C. kivuensis*.[20] Pouched rats are long lived and trainable species with an exceptionally large and well-developed olfactory bulb and primate-like neocortex, which comprise almost 20% and 75% of the total brain length and cerebral cortex, respectively.[12,19-21,28,30] Because of these features, pouched rats have been trained by nongovernmental organizations for olfactory detection of landmines, buried survivors of natural catastrophes, and diseases such as tuberculosis; they are also used for the study of olfaction.[6-8,23,24,30,31] Pouched rats are moreover a reservoir for monkeypox and used to study zoonotic disease.[10,11,25] Our institution established a colony of 65 *Cricetomys ansorgei* from a founder population of adult wild-caught animals imported from Tanzania in 2015. We maintain a colony for breeding and for research on olfactory physiology and the role of olfaction in mammalian social interaction and communication.[6-8]

Clinical literature on this species is scant; few publications are available on olfactory physiology or anatomic and clinical pathology in this species, and its spontaneous neoplasms and clinical care have not been reported.[2,6-8,19,22,28] This case report describes the occurrence of spontaneous pituitary neoplasms in 2 aged female Southern giant pouched rats.

Case Report

History. Both geriatric Southern giant pouched rats, hereafter referred to as pouched rats, were wild caught at an unknown age in Tanzania in October 2015 and were incorporated into the Cornell University pouched rat breeding and research colony at that time. The females were estimated to be at least 7.5 y of age; they were determined to be sexually mature and based on body size and appearance were over 6 mo old at the time of trapping. The pouched rats received yearly physical examinations based on colony standards for clinical care. They were also used regularly for experimental procedures, such as imaging or blood collection under isoflurane anesthesia. Between 2015 and 2022, the females were treated for minor clinical concerns, such as a 1-wk episode of diarrhea or mild dermatological issues that resolved uneventfully. Both pouched rats were also part of a study to evaluate the effects of diet on health of the colony. The clinical conditions reported herein were noticed in early 2023 by animal care staff.

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Clinical presentation. The first female pouched rat (case 1) was reported for poor coordination by animal care staff in January 2023. On veterinary examination, the female presented with vestibular deficits, including left-sided head tilt, ataxia, disorientation, and circling (Video S1). Despite a good appetite, the animal was underconditioned (body condition score 2/5) and moderately dehydrated and had pale extremities. The pouched rat also showed red-colored ocular discharge, orange-tinged, scaly, thin skin, and a sparse haircoat diffusely over the dorsum. Given the clinical findings, the differential diagnoses included inner or middle ear infection, neoplasia, hyper- or hypothyroidism, and hepatic neuropathy. Whole blood was collected from the midventral tail artery for a complete blood count, and biochemical and thyroid (T3, T4, and fT4) panels. A urinalysis was performed on a free catch urine sample.

The second pouched rat (case 2) was reported for polyuria and polydipsia by animal care staff in March 2023. On veterinary examination, the pouched rat was bright, alert, active, and responsive with a body condition score of 3/5 (good condition). The pouched rat had a mildly hunched posture but was adequately hydrated. Because of a previous occurrence of polyuria associated with diabetes mellitus in the colony, blood glucose was measured via glucometer over several days, and blood was submitted for biochemical analysis.

Materials and Methods

Animals. The Southern giant pouched rat colony was established in 2015 with wild-caught animals from a field site in Morogoro, Tanzania. Pouched rats were quarantined, tested according to requirements of the Center for Animal Disease Control and Prevention (Atlanta, GA), and treated for endo- and ectoparasites, as previously described.[28] The pouched rats were housed at AAALAC-accredited Cornell animal housing facilities in a negative pressure room at ABSL-2 conditions at 22 to 24 °C, 30% to 70% relative humidity, and 12:12-h light-dark cycle, consistent with *The Guide for the Care and Use for Laboratory* Animals.[13] Sexually mature pouched rats were housed individually in stainless steel cages with perforated stainless steel flooring, enriched with stainless steel huts and newspaper for nesting (24 in. long × 24 in. wide × 15.5 in. high; Hoeltge, Cincinnati, OH). Chlorinated, osmosis-purified, carbon-filtered water via automatic watering system was available ad libitum. Chow was also available ad libitum; the chow was changed from Teklad global 19% protein-extruded diet (Envigo, Indianapolis, IN) to 20% protein diet PicoLab Rodent Diet 20 5053 (ScottPharma Solutions, Marlborough, MA) in November 2022 for nonbreeding rats because of an increased incidence of suspected hepatopathies in the colony. This diet change occurred approximately 1 and 4 mo before euthanasia of cases 1 and 2, respectively. The 2 females in this report had been enrolled with 16 other pouched rats of different ages in a clinical study to analyze metabolic and microbiologic changes associated with this diet change via blood and feces collection in an IACUC approved protocol at Cornell University. The pouched rat colony undergoes yearly physical examinations. Further health monitoring and diagnostics are performed depending on clinical need.

Blood and urine sample collection and clinical pathology testing. Blood collection was performed in tandem with the study as mentioned above; therefore, blood biochemistry data for these pouched rats were available from November 2022, before the appearance of clinical signs and are listed in column "baseline" (Table 1). A second set of blood samples was collected with onset of clinical signs; in both cases, blood was collected from the midcentral tail artery with a 23-gauge needle butterfly (Winged Infusion Set; JORGENSEN LABS INC, Patterson Veterinary Supply, Devens, MA) into a 3-mL syringe (Monoject Sterile Syringe; CARDINAL HEALTH MED PROD+SER, Patterson Veterinary Supply, Devens, MA). Blood was then transferred into EDTA and nonanticoagulant tubes for complete blood count and biochemical analysis (Cobas 501; Roche Diagnostics) and thyroid testing. For case 1, blood was collected under general isoflurane anesthesia, induced at 5% in an induction box and maintained at 1.5% to 2.5%. For case 2, glucometer readings were performed in the conscious animal. The pouched rat was distracted with high-value treats placed under an overturned standard size rat cage with one edge removed, allowing for safe handling of the tail outside of the cage (Figure 1). Blood glucose was measured via AlphaTRAK 3 Blood Glucose Monitoring System Starter Kit (ZOETIS, Patterson Veterinary Supply, Devens, MA). Blood for biochemical analysis was collected into a nonanticoagulant similar to case 1. A free catch urine sample was collected from case 1, and a cystocentesis was performed immediately after euthanasia for case 2. All samples were submitted to the Cornell University Department of Population Medicine and Diagnostic Sciences, Animal Health Diagnostic Center for testing. The complete blood count and biochemical panel were done in the Clinical Pathology Laboratory. For the complete blood count, the sample was assayed with an automated hematology analyzer (ADVIA 2120i; Siemens Healthcare Diagnostics, Tarrytown, NY); a manual blood smear examination with differential cell count was done on a modified Wright's-stained smear (Hema-tek 1000, Siemens). The biochemical analysis was performed with a Cobas 501 analyzer (Roche Diagnostics, Indianapolis, IN), using manufacturer's reagents. For the urinalysis, urine specific gravity was measured with a Reichert Vet 360 TS refractometer, dipstick analysis was performed with a Clinitest Advantus (Siemens Healthcare Diagnostics), and a manual light microscopy examination was performed on the unstained urine sediment.

Thyroid hormone analysis was performed at the New York State Animal Health Diagnostic Center Endocrinology Section. Free T4 (FT4), total T4 (tT4), and total T3 (tT3) were analyzed with IMMULITE 2000 solid-phase, enzyme-labeled chemiluminescent competitive immunoassays, according to manufacturer's instructions (Immulite 2000 FT4, L2KFT42; tT3, L2KT36; L2KT42, Siemens) and assayed with IMMULITE 2000 XPi analyzer (Siemens).

MRI. MRI was performed under general anesthesia. Anesthesia was induced with combination of 4 mg/kg xylazine (Pivetal AnaSed (Xylazine) injection; Patterson Veterinary Supply, Devens, MA) and 80 mg/kg ketamine (KetaVed C IIIN; Vedco Inc., Patterson Veterinary Supply, Devens, MA) injected intraperitoneally and maintained by inhalation of 1.5% of isoflurane. The scans were obtained at the Cornell Magnetic Resonance Imaging Facility (CMRIF), Cornell University, Ithaca, New York and acquired on a 3.0T MRI (General Electric), using a small, 8-channel flex coil around the cranium in ventral recumbency. The following pulse sequence protocols were used with a phase array acceleration factor of 2 and a field of view of 12 cm: SAG T2 FSE 0.4 × 0.4 × 2.6–mm resolution, TR/TE = 4,632/120 ms, ETL = 21, 4 NEX; TS T2 FSE 0.4 × 0.4 × 2.6–mm resolution, TR/TE = 4,237/120 ms, ETL = 21, 4 NEX and TS T1 FSE 0.2 × 0.2 × 2.6–mm resolution, TR/TE = 948/11 ms, ETL = 3, 1.5 NEX.

Necropsy and sampling. Euthanasia was performed with barbiturate overdose via intraperitoneal injection (EUTHASOL pentobarbital sodium and phenytoin sodium; Virbac) under general anesthesia induced and maintained with isoflurane, as described above. Both pouched rats underwent routine

Table 1. Biochemical results from both southern giant pouched rats with established reference intervals for this species[28]

Chemistry						
Blood, whole, clotted						
	Case 1		Case 2		Reference interval	
Parameter	Baseline[a]	Clinical[a]	Baseline[a]	Clinical[a]		Units
Sodium	149	146	146	135	138–150	mEq/L
Potassium	5.2	4.7	4.9	4.8	4.1–5.8	mEq/L
Chloride	102	99	100	89	93–104	mEq/L
Bicarbonate	31	28	33	32	27–37	mEq/L
Anion gap	21	24	18	19	11–25	mEq/L
Na/K ratio	29	31	30	28	25–36	
Urea nitrogen	15	13	20	26	12–32	mg/dL
Creatinine	0.3	0.3	0.4	0.1	0.2–0.6	mg/dL
Phosphate	4.8	6.2	4.4	3.7	2.4–5.9	mg/dL
Total protein	6.8	6.8	6.5	7.2	6.2–8.7	g/dL
Albumin	3.3	2.8	3.2	3.4	2.2–3.4	g/dL
Globulin	3.5	4.0	2.2	3.8	3.2–6.4	g/dL
A/G ratio	0.9	0.7	1.0	0.9	0.4–1.0	
Glucose	101	142	194	417	101–209	mg/dL
ALT	28	37	21	24	12–58	U/L
AST	28	56	20	20	12–52	U/L
Alkaline phosphatase	48	47	67	61	49–164	U/L
Gamma glutamyl transferase	2	3	2	5	1–5	U/L
Total bilirubin	0.0	0.0	0.0	0	0–0.1	mg/dL
Amylase	1,086	1,202	815	982	512–1,096	U/L
Lipase	16	20	11	9	8–25	U/L
Cholesterol	133	247	114	128	71–205	mg/dL
Creatine kinase	313	310	136	276	231–607	U/L
Iron	197	282	222	126	84–322	µg/dL
Total iron-binding capacity	313	315	445	441	268–500	µg/dL
Iron saturation	63	90	50	29	24–78	%
Triglyceride	99	N/A	81	172	46–213	mg/dL

[a]Baseline: preclinical disease blood values were obtained in November 2022; clinical: postclinical disease blood values.

necropsies in left lateral recumbency. For case 1, for accurate characterization of the mass in situ, the whole skull was separated from the body at the level of the atlanto-occipital junction and placed in Formical-2000 Decalcifier, a combined decalcifying and fixative solution. The calvaria was delicately opened with rongeurs to allow efficient fixation of the brain. For case 2, no overt neurologic signs had been reported antemortem; therefore, the whole head was separated from the body and the calvaria was opened with rongeurs to expose the brain and allow fixation in situ. The head was submerged and fixed

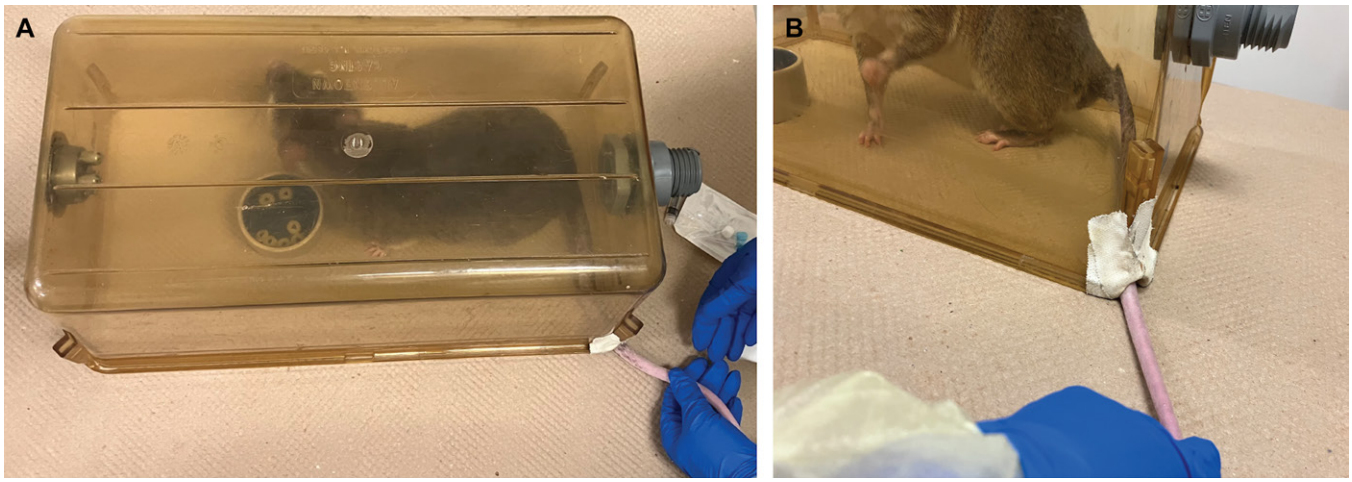

Figure 1. Restraint of African pouched rats for nonsedated blood draws. (A) African pouched rats are restrained with minimal contact beneath a standard size rat cage and distracted with high value treats. (B) A cut-out edge of the cage allows easy handling and blood draw in the conscious animal.

in 10% neutral buffered formalin for a week before removal and sectioning of the fixed brain.

Formalin-fixed paraffin-embedded tissue samples were routinely trimmed, processed, and stained with hematoxylin and eosin for light microscopic examination. The tissues were processed for immunohistochemical staining with an anti–thyroid-stimulating hormone (TSH) (recombinant mouse monoclonal antibody, clone A-10; Huabio, Woburn, MA) and anti-PRL (mouse monoclonal antibody, clone 6F11; Invitrogen, Waltham, MA) antibody using the Leica Bond Max Automated Immunohistochemistry Staining System, according to the manufacturer's instructions (Leica Microsystems, Buffalo Grove, IL). Before proceeding with immunohistochemical staining, tissues were sectioned at 5.0 µm and deparaffinized with Bond Dewax Solution (Leica, Buffalo Grove, IL). Pretreatment with heat-induced epitope retrieval was performed for 20 min (TSH) and 30 min (PRL), respectively, using a citrate-based pH 6 epitope retrieval solution (Bond Epitope Retrieval Solution 1; Leica Microsystems, Buffalo Grove, IL). Endogenous peroxidase activity was blocked with a 3% peroxide solution for 5 min (Leica Microsystems, Buffalo Grove, IL). The anti-TSH antibody was diluted at 1:200 and applied to the slides for 60 min, while the anti-PRL antibody was diluted at 1:100 and applied to the slides for 15 min. PowerVision Poly-Horseradish Peroxidase Anti-Mouse IgG reagent was then applied to the slides for 30 min (TSH) and 10 min (PRL), respectively (Leica Microsystems, Buffalo Grove, IL). Subsequently, tissues were developed with 3,3-diaminobenzidine chromogen (Leica Microsystems, Buffalo Grove, IL) for 10 min. The slides were finally counterstained with hematoxylin (Leica Microsystems, Buffalo Grove, IL) for 5 min, and successively dehydrated, cleared, and mounted. For negative controls, antibody diluent replaced the primary antibodies. Remnant pituitary tissue in the second pouched rat was used as an internal positive control for both pouched rats and appropriately showed cytoplasmic immunolabeling both for TSH and PRL.

Results

Clinical diagnostic findings and interpretation. For case 1, external and otoscopic exam of the ear did not reveal any clinical abnormalities. The complete blood count (data not shown) was within reference intervals[28] and blood biochemical analysis after the onset of disease revealed mild changes as compared with baseline samples that had been collected as part of the dietary change study in November 2022 (Table 1). The total and free T4 were within normal limits, whereas the T3 concentration was mildly above the range of values obtained from 16 clinically healthy pouched rats (Table 2). This finding was interpreted as potential hyperthyroidism. The urinalysis was within normal limits (Table 3). Although the pouched rat received supportive fluid therapy with 60 mL prewarmed lactated ringers (ICU Medical Inc., Patterson Veterinary Supply, Devens, MA), was treated with Enrofloxacin (20 mg/kg) (Pivetal Fluroxin Injection for Dogs 2.27%; Patterson Veterinary Supply, Devens, MA) per os (by mouth) for presumptive otitis and was placed on a critical care diet (Critical Care Omnivore; OXBOX Animal Health, Patterson Veterinary Supply, Devens, MA) for 7 days, the vestibular signs persisted. An intracranial lesion was suspected, and MRI was performed. A large, round, circumscribed mass was identified in the middle and caudal cranial fossa, centered on the pituitary fossa, and extending into the suprasellar space (Figure 2A, B).

The mass had heterogeneous T2- and T1-weighted hypointensity and hyperintensity, including a large, irregular, focal region rostrally of the T2 and T1 hypointensity. These findings likely represented hemorrhage of variable chronicity. The mass severely displaced and compressed the brain stem, thalamus, third ventricle, cerebrum, and cerebellum. The caudoventral aspect of the cerebellum was protruding through the foramen magnum. The region of the pituitary gland was effaced by the mass. There was no evidence of concurrent inner ear disease. Both lateral ventricles, the third ventricle, and the fourth ventricle cranial to the lateral apertures were mild-to-moderately dilated. In addition, the imaged portion of the cervical spinal cord had a severe, locally extensive, T2-weighted hyperintensity that was more severe centrally. The clinical signs were attributed to increased intracranial pressure from the mass. The primary differential diagnosis was a large pituitary neoplasm resulting in obstructive hydrocephalus and syringohydromyelia. Given the heterogeneous mixed intensity, including the region of T2 and T1 hypointensity, pituitary hemorrhage of varying chronicity was suspected, possibly causing apoplexy. Other causes of suprasellar masses (e.g., meningioma, round cell neoplasia) were considered less likely. In common rat strains and other domestic species, including dogs, this pattern is mostly consistent with a pituitary macroadenoma[15] with a further classification

Table 2. Thyroid panel results from clinical case 1

Thyroid panel			
Blood, whole, clotted			
Parameter	Result	Expected normal*	Units
T3	170	60–150	ng/dL
T4	3.34	0.96–4.74	µg/dL
fT4	0.949	0.59–1.12	ng/dL

*Upper and lower limit (range, mean ± 2 SD) of results from 16 unrelated clinically healthy sexually mature pouched rats between 6 months and under 1 y of age and consisting of 5 aged females (born before 2018), 3 middle aged females and 2 middle aged males (born after February 2018), and 3 weaned, sexually immature females and males, respectively. One of the rats was a wild-caught female; the others were bred in house.

Table 3. Urinalysis results from both southern giant pouched rats in this study

Urine analysis		
Urine, 2.0 mL		
	Case 1	Case 2
Color	Light yellow	Colorless
Turbidity	Clear	Clear
Specific gravity	1.017	1.005
pH	7.5	7.0
Protein	100 (2+) mg/dL	100 (2+) mg/dL
Glucose	Negative	≥1,000 (large) mg/dL
Ketones	Negative	Negative
Bilirubin	Negative	Negative
Heme	Negative	Trace
WBC	<5/HPF*	<5/HPF*
RBC	<5/HPF*	<5/HPF*
Bacteria	None seen	None seen
Epithelial cells	Very few	Very few
Fat drops	None seen	None seen
Debris	Moderate	None seen
Casts	None seen	None seen
Crystals	Amorphous–moderate	Amorphous–moderate

*HPF High power field.

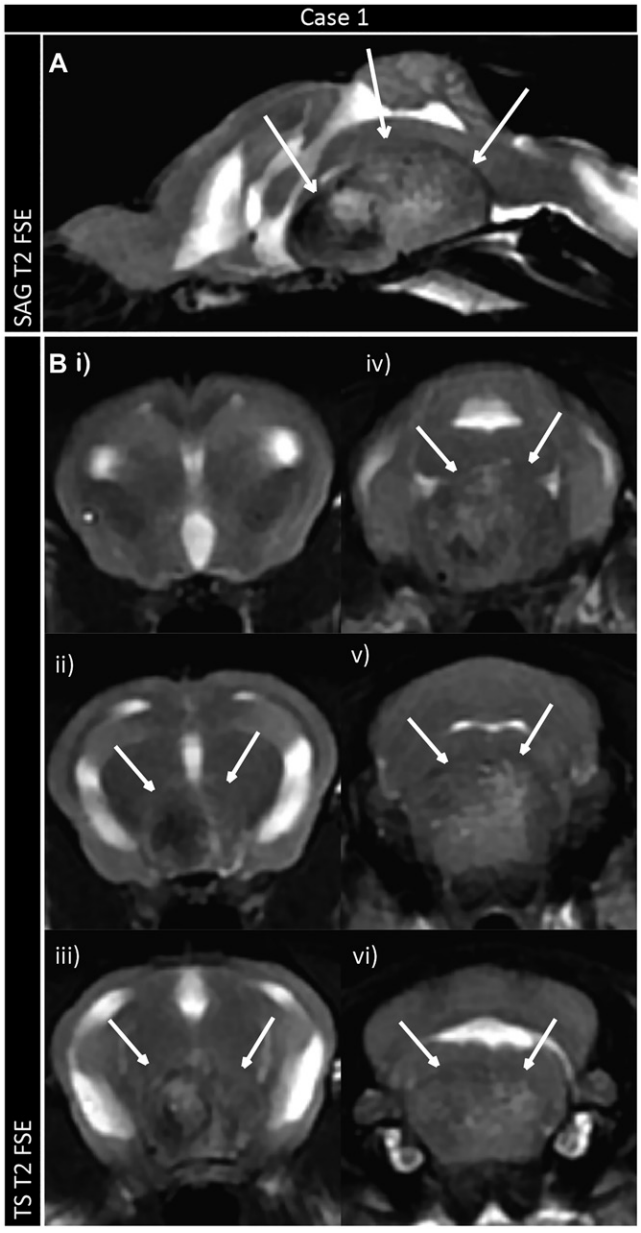

Figure 2. Representative MRI images of the head of case 1. (A) In the T2-weighted fast spin echo (FSE) sagittal (SAG) image of the head, a mass was identified (outlined with white arrows). (B) Serial transverse sections of T2-weighted FSE images of the head from cranial (top left, i) to caudal (bottom right, vi), the mass first appears in image i) mass and is outlined by white arrows in ii) to vi).

of a presumptive hormone-producing macroadenoma due to clinically observed dermatopathy. An infectious/immune mediated granulomatous disease at this location was considered unlikely. Because of the poor prognosis and ineligibility for continuation in the study, euthanasia was performed by using intraperitoneal injection of barbiturate under general anesthesia, and a diagnostic necropsy was performed.

Case 2 presented with polyuria and polydipsia. A persistently increased blood glucose concentration (471 and 512 mg/dL) was documented over 2 consecutive days with the glucometer. This result was confirmed by the serum biochemical analysis (Table 1). These results were interpreted as presumptive diabetes mellitus. Previous cases of diabetes mellitus in the pouched rat colony were treated with metformin (125 to 500 mg once a day to twice a day [Rx Generics, Metformin HCl Tablets; Patterson Veterinary Supply, Devens, MA]) depending on severity of clinical signs. However, because of the age of the animal and subsequent exclusion from research, euthanasia under general anesthesia and a postmortem examination were performed. A urine sample collected by cystocentesis after euthanasia revealed hyposthenuric urine (specific gravity of 1.005) and marked glucosuria (>1,000 mg/dL), consistent with diabetes mellitus. (Table 3).

Pathologic findings. ***Case 1.*** External examination of the body of case 1 at necropsy revealed poor haircoat quality, characterized by patchy hypotrichosis, coarseness, and scattered keratinaceous casts (also noted on antemortem exam). Moderate enlargement of the left and right inguinal mammary glands with release of thin, opaque, light yellow to white milky fluid on section was also seen. Based on clinical and imaging findings, the whole head was decalcified and fixed in 10% neutral-buffered formalin with the brain in situ. Serial sections of the decalcified head confirmed the presence of a 1.0-cm-diameter pituitary mass that significantly elevated and compressed the brain (Figure 3A). Moderate hydrocephalus was evident, correlating with the imaging results. Histologically, the mass consisted of cords and trabeculae of polygonal eosinophilic cells amid thin fibrovascular stroma, often organized in pseudorosettes surrounding congested, thin-walled vessels (Figure 3B). A moderate degree of atypia was observed throughout, characterized by anisokaryosis and anisocytosis, and occasional cytomegaly and karyomegaly. Mild mitotic activity was noted (5 mitotic figures in ten 400× fields or 2.37 mm^2) (Figure 3C). Differentiating pituitary adenomas from carcinomas mainly relies on the presence or absence of basisphenoid bone and/or brain invasion.[3] Case 1 had basisphenoid invasion (Figure 3B) with neoplastic nests infiltrating the bone into the underlying striated skeletal muscle, supporting a diagnosis of carcinoma over adenoma. Immunohistochemical staining of formalin-fixed paraffin-embedded sections of the mass revealed marked cytoplasmic immunolabeling for PRL and no immunolabeling for TSH, prompting a diagnosis of prolactinoma (Figure 3D).

Histologic examination of the middle and inner ear of the first pouched rat revealed mild compression of the left vestibulocochlear nerve and spiral ganglion but no overt evidence of alteration of the vestibular and auditory structures; this suggests that compression of the neuroparenchyma caused the vestibular deficits rather than primary peripheral vestibular disease or extension of the process to the inner ear or middle ear.

Mammary hyperplasia with active lactation was confirmed on combined gross examination and histology. Light microscopy strengthened, the diagnosis of hyperplasia by showing mammary acinar ectasia, overt epithelial cytoplasmic microvacuolation with variable hypertrophy, and rare loss of polarity and occasional thickening of the epithelium up to 2 cells thick. The mammary acini were frequently filled with proteinaceous secretory fluid, consistent with production of milk, which was attributed to excess PRL production from the tumor.

Histologic examination of representative skin sections of case 1 revealed features of atrophic dermatopathy. The features of atrophic dermatopathy were primarily hyperkeratosis, epidermal thinning, sparsely distributed cutaneous adnexa, and excessive trichilemmal keratinization. However, the histologic features of the skin of pouched rats has not been characterized in the literature; therefore, our evaluation of the hair cycle and its likely anomalies is speculative and based on comparison with textbook features of endocrine dermatopathy in other veterinary species.[14] The cause of the skin changes was not identified, but they ultimately were not attributed to the pituitary tumor.

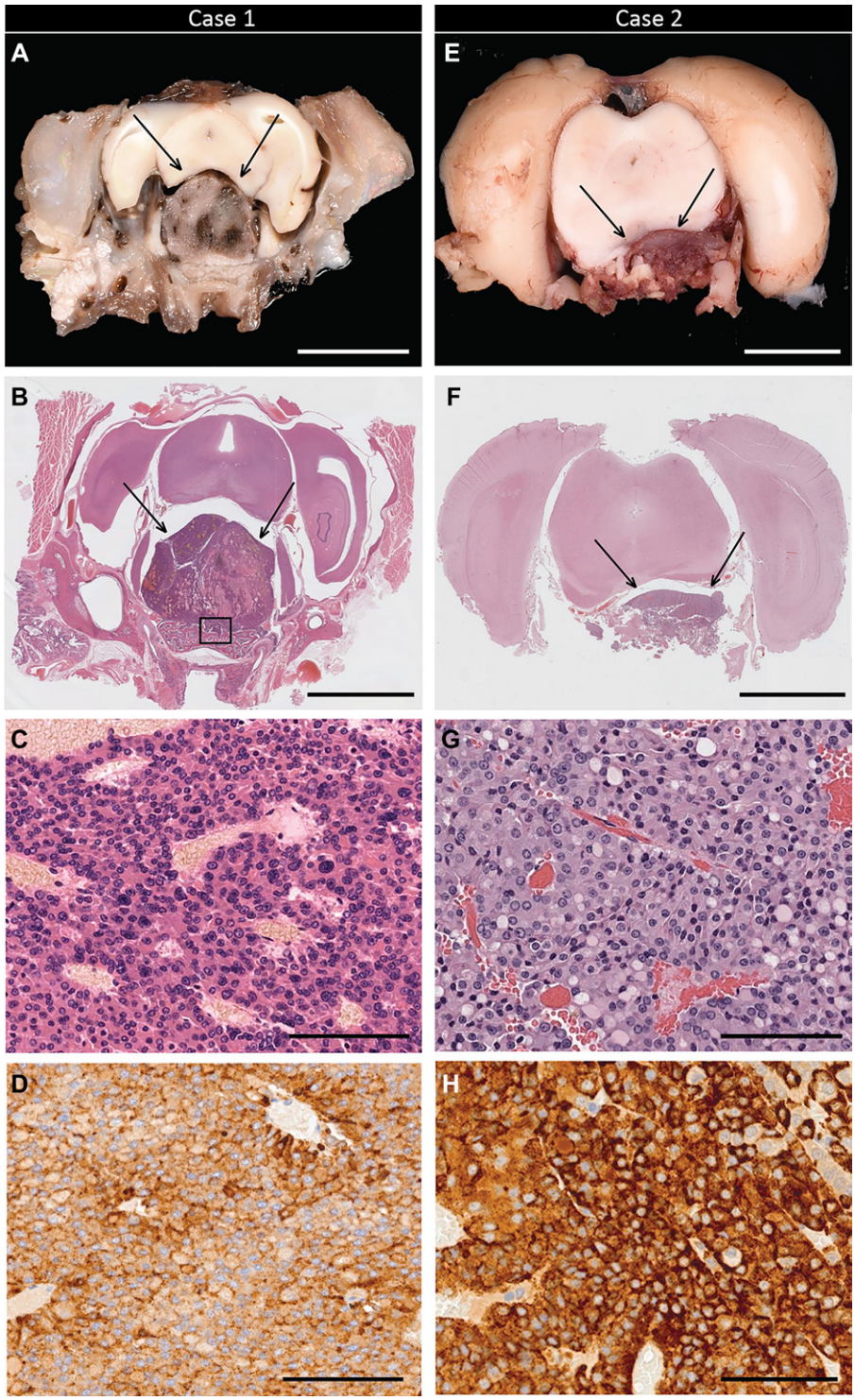

Figure 3. Representative gross and histopathologic images of the pituitary neoplasm of case 1 and case 2. (A) Transverse section of the skull with brain and pituitary gland in situ. Scale bar: 1.0 cm. An ovoid, expansile mass (arrows) compresses and elevates the overlying brain (case 1). (B) Skull with brain and pituitary gland, hematoxylin and eosin (H&E). Scale bar: 1.0 cm. The mass (arrows) is densely cellular and has a variegated appearance imparted by congested intratumoral sinusoids. Neoplastic cells invade the underlying basosphenoid bone (square) (case 1). (C) Detail of the neoplastic cells, H&E. Scale bar: 100 µm. Tightly arranged cords of polygonal cells amid delicate fibrovascular stroma surround congested intratumoral capillaries and sinusoids (case 1). (D) Neoplastic cells with strong cytoplasmic immunolabeling for prolactin (PRL). Scale bar: 100 µm. (E) Transverse section of brain and pituitary gland. Scale bar: 0.5 cm. A compressive, solid plaque-like mass (arrows) arises from the region of the pituitary gland and elevates the overlying thalamus. Scale bar: 100 µm (case 2). (F) Brain and pituitary gland, H&E. Scale bar: 0.5 cm. On light microscopy, the mass (arrows) appears densely cellular and noninvasive (case 2). (G) Detail of neoplastic cells, H&E. Scale bar: 100 µm. Neoplastic cells form packets and trabeculae of plump polygonal cells often bearing a single intracytoplasmic macrovacuole and surrounding congested capillary and sinusoids (case 2). (H) Neoplastic cells have strong cytoplasmic immunolabeling for PRL. Scale bar: 100 µm.

Case 1 also had bilateral chronic nephropathy, a common incidental age-related lesion of rodents.

Case 2. Because case 2 showed no overt neurologic signs before necropsy, an intracranial mass was not suspected based on clinical signs, and therefore the skull was not processed with the brain in situ, as had been done for case 1. Therefore, bone invasion could not be used to differentiate adenoma and carcinoma. On gross examination, a solid, plaque-like mass (1.3 × 0.7 × 0.4 cm) was identified that caused moderate elevation and compression of the brain (Figure 3E). The mass extended from the optic chiasm to the level of the medulla oblongata (Figure 3F). On histologic examination, the neoplastic cells resembled those seen in case 1 and consisted of packets and trabeculae of light eosinophilic, polygonal cells amid fibrovascular stroma, sparsely forming perivascular pseudorosettes (Figure 3G). The degree of atypia in this tumor was judged to be mild as compared with case 1. Given the relative homogeneity of the neoplastic cells, their mild degree of atypia, minimal mitotic activity (<1 in ten 400× fields or 2.37 mm^2), and the absence of brain invasion in the examined sections, a diagnosis of adenoma was favored. Immunohistochemical staining of formalin-fixed paraffin-embedded sections of the mass revealed similar results to case 1, with marked cytoplasmic immunolabeling for PRL and no immunolabeling for TSH (Figure 3H).

Concurrent mammary hyperplasia that was not evident grossly was also identified histologically in case 2. Mammary glands were variably hyperplastic, tortuous, and branching and contained moderate amounts of milk, as seen in case 1, supporting active production of PRL by neoplastic cells in both cases. Thorough gross and histologic evaluation of the pancreas of the second pouched rat did not reveal any significant findings that would have correlated with the clinical diagnosis of diabetes mellitus.

Discussion

This case report describes the occurrence of pituitary neoplasia in 2 geriatric pouched rats (*Cricetomys ansorgei*), only one of which displayed neurologic signs that could be attributed to the aggressive nature of the tumor and subsequent local brain changes. Although the literature contains no specific information on pituitary tumors in pouched rats, spontaneous pituitary tumors are a common, well-documented tumor of aged research and domestic mice and rats and may be clinically overt or quiet, as seen in the 2 cases described here.[1,18] A previous study reported that proliferative lesions of endocrine cells of the pituitary gland occurred in rat strains, such as Wistar/Furth and Ico, with an incidence of 38% in rats older than 10 mo.[29] This finding is consistent with another study that screened 736 rats of 6 different strains, including F344, Wistar/Slc, Sprague-Dawley and others, and reported a similar incidence of spontaneous pituitary tumors in rats between 1 to 2 y of age.[18] Another study reported higher evidence of pituitary neoplasms in males than females (85% and 79%, respectively) conflicting with 2 other reports.[17,26,29] To date, we have not identified pituitary neoplasms in males in our pouched rat colony, which might be due to a higher incidence of proliferative pituitary lesions in female pouched rats, as occurs in strains of *Rattus norvegicus* and *Mus musculus*.[1,26,29] However, all of the aged pouched rats currently in our colony are females; further studies and postmortem analysis are required to understand possible sex predisposition of pituitary neoplasms in this species.

Proliferative pituitary lesions are most commonly described as benign adenomas in C57Bl/6, Swiss, and FBV/N mice and in various rat strains, consistent with the histologic presentation of case 2 in our report.[1,5,18] However, in case 1, evidence of local bone and muscle invasion supported a diagnosis of pituitary carcinoma rather than adenoma, and vestibular signs in case 1 were presumptively attributed to compression of the left vestibulocochlear nerve, as seen in histopathologic assessment of the tumor and further supporting an invasive carcinoma.

PRL-producing pituitary neoplasms, or prolactinomas, are the predominant subtype of pituitary neoplasms in various strains of *Rattus norvegicus* and *Mus musculus*.[1,4,16,29] Pituitary neoplasms in Long Evans rats are most often prolactinomas, followed by luteinizing hormone-producing tumors; other pituitary neoplasms are TSH, growth hormone, adrenocorticotropic hormone–producing tumors (or a combination thereof), or non-immunostaining tumors.[16] This high incidence of prolactinomas in rats is consistent with previous findings in mice and with the 2 cases we describe.[1] Elevated T3 levels in conjunction with dermatological changes in case 1 initially raised consideration of a TSH-producing neoplasm, but neoplasms in both cases lacked TSH expression. Active production of PRL by neoplastic cells is considered to have caused mammary hyperplasia and active lactation in both of our cases, as previously reported in rats.[25]

This report documents an extensive clinical work up including complete blood count, blood biochemistry analysis, urinalysis, MRI, and subsequent correlation to gross and histopathologic findings in an understudied species. Although pituitary adenomas far outnumber pituitary carcinomas in rats and mice routinely used in research settings, the relative prevalence of adenomas and carcinomas in pouched rats remains yet to be determined. We are unaware of other spontaneous tumors that develop in aged pouched rats. Similar future comprehensive reports will aid in better characterizing Southern giant pouched rats and will expand and strengthen the literature related to the clinical care of this and other *Cricetomys* species.

Supplemental Material

Video S1. Clinical presentation of pouched rat from case 1. The pouched rat presented with vestibular deficits as characterized by ataxia and head tilt.

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References

1. **Barthold SW, Griffey SM, Percy DH.** 2016. Pathology of laboratory rodents and rabbits, 4th ed. West Sussex (England): Wiley-Blackwell. https://doi.org/10.1002/9781118924051.
2. **Bentz EJ, Ophir AG.** 2022. Chromosome-scale genome assembly of the African giant pouched rat (*Cricetomys ansorgei*) and evolutionary analysis reveals evidence of olfactory specialization. Genomics **114**:110521. https://doi.org/10.1016/j.ygeno.2022.110521.
3. **Brändli-Baiocco A, Balme E, Bruder M, Chandra S, Hellmann J, Hoenerhoff MJ, Kambara T, et al.** 2018. Nonproliferative and proliferative lesions of the rat and mouse endocrine system. J Toxicol Pathol **31** 3_Suppl:1S–95S. https://doi.org/10.1293/tox.31.1S.
4. **Doi T, Kanno T, Sato J.** 2021. Histopathological and immunohistochemical features of proliferative lesions in the pituitary pars distalis of rats. J Toxicol Pathol **34**:1–9. https://doi.org/10.1293/tox.2020-0050.
5. **el Etreby MF, Lorenz B, Habenicht UF.** 1988. Immunocytochemical studies on the pituitary gland and spontaneous pituitary tumors of Sprague-Dawley rats. Pathol Res Pract **183**:645–650. https://doi.org/10.1016/S0344-0338(88)80033-5.

6. **Freeman AR, Ophir AG.** 2018. Scent-marking behavior of the southern giant pouched rat (*Cricetomys ansorgei*). J Mammal **99**:1430–1435. https://doi.org/10.1093/jmammal/gyy137.
7. **Freeman AR, Ophir AG, Sheehan MJ.** 2020. The giant pouched rat (*Cricetomys ansorgei*) olfactory receptor repertoire. PLoS One **15**:e0221981. https://doi.org/10.1371/journal.pone.0221981.
8. **Freeman AR, Sheehan MJ, Ophir AG.** 2019. Anogenital distance predicts sexual odour preference in African giant pouched rats. Anim Behav **148**:123–132. https://doi.org/10.1016/j.anbehav.2018.12.010.
9. **Huchon D, Chevret P, Jordan U, Kilpatrick CW, Ranwez V, Jenkins PD, Brosius J, Schmitz J.** 2007. Multiple molecular evidences for a living mammalian fossil. Proc Natl Acad Sci USA **104**:7495–7499. https://doi.org/10.1073/pnas.0701289104.
10. **Hutin YJ, Williams RJ, Malfait P, Pebody R, Loparev VN, Ropp SL, Rodriguez M, et al.** 2001. Outbreak of human monkeypox, Democratic Republic of Congo, 1996 to 1997. Emerg Infect Dis **7**:434–438. https://doi.org/10.3201/eid0703.017311.
11. **Hutson CL, Nakazawa YJ, Self J, Olson VA, Regnery RL, Braden Z, Weiss S, et al.** 2015. Laboratory investigations of African pouched rats (*Cricetomys gambianus*) as a potential reservoir host species for monkeypox virus. PLoS Negl Trop Dis **9**:e0004013. https://doi.org/10.1371/journal.pntd.0004013.
12. **Ibe CS, Onyeanusi BI, Hambolu JO.** 2014. Functional morphology of the brain of the African giant pouched rat (*Cricetomys gambianus* Waterhouse, 1840). Onderstepoort J Vet Res **81**:e1–e7. https://doi.org/10.4102/ojvr.v81i1.644.
13. **Institute for Laboratory Animal Research.** 2011. Guide for the care and use of laboratory animals, 8th ed. Washington (DC): The National Academies Press.
14. **Mauldin EA, Peters-Kennedy J.** 2016. Integumentary system, p 509–736.e1. In: Grant Maxie M, editor. Jubb, Kennedy Palmer's Pathology of Domestic Animal, vol. **1**. St. Louis, Missouri, 2016: Elsevier.
15. **Mayer J, Sato A, Kiupel M, DeCubellis J, Donelly T.** 2011. Extralabel use of cabergoline in the treatment of a pituitary adenoma in a rat. J Am Vet Med Assoc **239**:656–660. https://doi.org/10.2460/javma.239.5.656.
16. **McComb DJ, Hellmann P, Kovacas K, Scott D, Evans WS, Burdman JA, Thorner MO.** 1985. Spontaneous sparsely-granulated prolactin-producing pituitary adenomas in aging rats: a prospective study of the effect of bromocriptine. Neuroendocrinology **41**:201–211. https://doi.org/10.1159/000124179.
17. **McComb DJ, Kovacas K, Beri J, Zak F.** 1984. Pituitary adenomas in old Sprague-Dawley rats: a histologic, ultrastructural, and immunocytochemical study. J Natl Cancer Inst **73**:1143–1166.
18. **Nagatani M, Miura K, Tsuchitani M, Narama I.** 1987. Relationship between cellular morphology and immunocytological findings of spontaneous pituitary tumors in the aged rat. J Comp Pathol **97**:11–20. https://doi.org/10.1016/0021-9975(87)90122-8.
19. **Nzalak JO, Byanet O, Salami SO, Umosen AD, Maidawa SM, Ali MN, Imam J.** 2008. Comparative morphometric studies of the cerebellum and forebrain of the African giant rat (AGR) (*Cricetomys gambianus*-waterhouse) and that of grasscutter (*Thryonomys swinderianus*). J Anim Vet Adv **7**:1090–1092.
20. **Olayemi A, Nicolas V, Hulselmans J, Missoup AD, Fichet-Calvet E, Amundala D, Dudu A, Dierckx T, Wendelen W, Leirs H, Verheyen E.** 2012. Taxonomy of the African giant pouched rats (Nesomyidae: Cricetomys): molecular and craniometric evidence support an unexpected high species diversity. Zool J Linn Soc **165**:700–719. https://doi.org/10.1111/j.1096-3642.2012.00823.x.
21. **Olude MA, Mustapha OA, Ogunbunmi TK, Olopade JO.** 2013. The vertebral column, ribs, and sternum of the African giant rat (*Cricetomys gambianus* waterhouse). ScientificWorldJournal **2013**:1–5. https://doi.org/10.1155/2013/973537.
22. **Onwuke SK, Nssien SK, Olayemi FO, Olusola A.** 2003. Further studies on the plasma biochemistry of the African giant rat (*Cricetomys gambianus*, Waterhouse). Afr J Biomed Res **6**:33–36.
23. **Poling A, Mahoney A, Beyene N, Mgode G, Weetjens B, Cox C, Durgin A.** 2015. Using giant African pouched rats to detect human tuberculosis: a review. Pan Afr Med J **21**:1–6. https://doi.org/10.11604/pamj.2015.21.333.2977.
24. **Poling A, Weetjens BJ, Cox C, Beyene N, Bach H, Sully A.** 2010. Geneva International Center for Humanitarian Demining, Geneva. Behav Anal Pract **3**:19–25. https://doi.org/10.1007/BF03391761.
25. **Reynolds MG, Carroll DS, Olson VA, Hughes C, Galley J, Likos A, Montgomery JM, et al.** 2010. A silent enzootic of an orthopoxvirus in Ghana, West Africa: evidence for multi-species involvement in the absence of widespread human disease. Am J Trop Med Hyg **82**:746–754. https://doi.org/10.4269/ajtmh.2010.09-0716.
26. **Son WC.** 2004. Factors contributory to death of young Sprague-Dawley rats in carcinogenicity studies. Toxicol Lett **153**:213–219. https://doi.org/10.1016/j.toxlet.2004.03.024.
27. **Steppan SJ, Schenk JJ.** 2017. Muroid rodent phylogenetics: 900-species tree reveals increasing diversification rates. PLoS One **12**:e0183070.
28. **Stokol T, Brandt LE, Shuman M, Jeffery DA, Blank B, Silvela E, Singh B.** 2021. Hematologic and biochemical reference intervals and urinary test results for wild-caught adult southern giant pouched rats (*Cricetomys ansorgei*). J Am Assoc Lab Anim Sci **60**:616–629. https://doi.org/10.30802/AALAS-JAALAS-20-000154.
29. **Trouillas J, Cirod C, Claustrat B.** 1982. Spontaneous pituitary tumors in the Wistar/Furth/Ico rat strain. An animal model of human prolactin adenoma. Am J Pathol **109**:57–70.
30. **Verhagen R, Cox C, Machangu R, Weetjens B, Billet M.** 2003. Preliminary results on the use of Cricetomys rats as indicators of buried explosives in field conditions. Mine Detectection Dogs Training. p 175–193. Available at: https://chiron-k9.com/wp-content/uploads/2017/11/MDD.pdf
31. **Weetjens BJC, Mgode GF, Machang'u RS, Kazwala R, Mfinanga G, Lwilla F, Cox C, et al.** 2009. African pouched rats for the detection of pulmonary tuberculosis in sputum samples. Int J Tuberc Lung Dis **13**:737–743.

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