Hyperzincaemia in a pet African giant rat (*Cricetomys gambianus* Waterhouse, 1840)

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ABSTRACT

Presented is an African giant rat (*Cricetomys gambianus*) following zinc ingestion. The sick rat was lethargic, withdrawn, had soft, mucus-impregnated faeces and diahorrea, foot twitching and icterus. Comparative age, sex and body weight (b.wt.)-matched analyses were made with a healthy giant rat. Twelve-hourly Urine volume (UV), Haematocrit (Hct), urinary glucose, plasma zinc and Alkaline Phosphatase (ALP) were performed over an 8-week period. Full blood counts were performed and differential WBC counts and microscopic observations were made on blood smears obtained from both healthy and sick rats. Consecutive blood samples were drawn at the end of each week (Weeks <2–6 treatment; Weeks 7–8 post-treatment). Treatment involved oral vitamin B_{12} supplement at 4 μg/day and 2 mℓ diethylenetriaminepentaacetic acid (DTPA) intramuscular injections at 1 mℓ/450g b.wt./5 wks (Week 2 – 6). Day 1 showed neutropaenia, Heinz bodies on RBCs (reticulocytes and immature forms). Zinc (Day 1 – end Week 7), glucose (Day 1 – end Week 4), ALP (Day 1 – Week 4) and UV were elevated (Day 1 – end Week 6). Indications of moderate zinc toxicosis following ingestion and stress-associated glucosuria were concluded.

Key words: African giant rat, *Cricetomys gambianus,* glucosuria, gnawing, hyperzincaemia, pet.

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INTRODUCTION

The African giant rat or the Gambian pouched rat, *Cricetomys gambianus* (Order: Rodentia; Family: Nesomyidae) is the world's largest nocturnal rat and is native to Africa, many thriving in urban settings[1,7]. They live up to 8 years in captivity reaching maximum body weights of approximately 2.8 kg in bucks and 1.39 kg in does. They have become extremely popular as exotic pets and are used to detect landmines. Field observations and notes on the behaviour and domestication of this rat have been published[1–3,6].

Chronic zinc ingestion has been reported to cause copper deficiency and anaemia as a consequence of the intestinal interaction of zinc and copper[34]. Acute zinc poisoning is reflected in a haemolytic crisis with renal, gastrointestinal and hepatic dysfunction[37].

This is a case report of a 2-year, 9-month-old female pouched rat (897.21 g b.wt.) poisoned by chronic ingestion of zinc from gnawing activity on a cage.

MATERIALS AND METHODS

The sick giant rat was housed in the Animal house at West Bar Veterinary Hospital, Banbury, UK (temperature 23 °C; RH 37 %; 24 h light/24 h dark cycle). The healthy rat was housed in a North Kent Plastics (NKP) metabolism cage, Dartford, Kent, UK. Food, including Mouse Comproids, boiled chicken, vegetables, and water were provided *ad libitum.* The healthy rat was only used to compare initial basal values at diagnosis. Due to expense of rats and ethics, only 2 rats were observed in the current study. Urine volume presented as mean ± standard error of the mean (s.e.m.) was determined from 12-hour collections over an 8-week period. Day 1 was taken as the day of diagnosis. A venous tail blood sample (1 mℓ) was collected (Day 1, Table 1), cooled in a heparinised tube, centrifuged at 10 000 rpm and subjected for haematological and biochemical analyses. Haematocrit (Hct) was determined by microcentrifugation, a 2-Drop Clinitest (Bayer Diagnostic) with glucose sensitivity accurate over 1 g/ℓ was used for urinary glucose determination[11,39] and plasma zinc determinations were made by spectrophotometric analysis[38]. Red blood cells (RBC) and white blood cells (WBC) were counted with a haemocytometer (Gilson Microman, Anachem, UK), and blood smears were stained with Giemsa stain for differential leukocyte counts[25]. Optical microscopic observations of RBC were made at ×400 magnification. Alkaline phosphatase (ALP) was measured with a kit (Telechem International Inc., ArrayIt® Division, Sunnyvale, USA). The assay used quantitative colorimetric analysis on sample sizes of 200 $\mu\ell$. The test was based on the conversion of para-nitrophenylphosphate (p-NPP) to para-nitrophenol and the colorimetric determination of the resulting coloured product. The test system was optimised with respect to substrate concentration, and reaction time. The obtained values were converted to quantitative results through a standard curve created using commercial ALP. Consecutive blood samples were collected every 7 days after Day 1 over a 7-week period subdivided into Week 2–6 treatment and Week 7–8 post-treatment periods (Table 1). Treatment was administered 1 hour following diagnosis. The diagnosis was made 2 days following the onset of sickness. Treatment included vitamin B_{12} supplement orally at 4 μg/day[11] and 2 mℓ diethylenetriaminepentaacetic acid (DTPA)[9] injections administered intramuscularly at a dose of 1 mℓ/450 g b.wt. for 5 weeks (Week 2–6). Vitamin B_{12} was administered to stimulate erythropoeisis and as a hepatic stimulant for processing haemoglobin[36]. An extensive search of the literature revealed 3 studies on the haematological parameters of the giant rat[10,20,26]. Results from these studies were used to establish the normal parameters of haematology in the current investigation. Handling and experimentation were in strict accordance with the stipulations in Animals (Scientific Procedures) Act of 1986 (UK). There was no need for an ethics approval protocol as the study was a clinical case report. All data were compared between sick rat and healthy rat, and, where appropriate, acceptable reference intervals were considered.

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Table 1: **Biochemical, haematological and fluid balance parameters measured at the end of each week in an African giant rat chronically exposed to zinc during treatment over 6 weeks with vitamin B_{12} and DTPA, and a 2-week post-treatment period.**

Parameter	Treatment at the end of the week						Post-treatment	
	Day 1 (Week 1)	Week 2	Week 3	Week 4	Week 5	Week6	Week 7	Week 8
Zn^{2+} (67.0 µ g/100mℓ) [a]	172.8*	165.6*	134.3*	126.6*	103.9*	98.1*	82.0*	70.0
Urinary glucose (0.0 g/ℓ)	4.2*	1.7*	1.4*	1.1*	0	0	0	0
ALP (79.0 UI/ℓ)	133.0*	120.0*	101.0*	90.0*	82.0	80.0	79.0	79.0
Hct (40.0%)	31.0*	32.0*	34.0*	38.5	40.0	40.0	40.0	40.0
Mean (sem) UV (6 ± 1 mℓ/h)	12 (1)*	14 (2)*	13 (1)*	12 (2)*	10 (1)*	9 (2)*	6 (2)	5.8 (2)

[a]Baseline value obtained from a healthy rat.
*Comparative differences between healthy and sick rats.

RESULTS

Approximate b.wt. were 897.21 g for the sick rat and 908.32 g for the healthy rat. Initial observations of the sick rat showed that it was lethargic, withdrawn and passing soft, mucus-impregnated faeces interspersed with diahorrea. Foot twitching and icterus were observed in the hind legs and mouth, respectively. The rat had been anorexic for 3 days. The urine was not discoloured. Where appropriate, values were presented in comparison with minimum and maximum values, and a reference value from previous haematological investigations in this species.

Haematological analyses on Day 1 demonstrated an anaemia with a RBC count of 4.95 × $10^9/ℓ$ (reference interval: 5.5–11.0 × $10^9/ℓ$) by comparison with previous findings of 5.49 × $10^9/ℓ$[26]; an attenuated WBC count of 4.20 × $10^9/ℓ$ (reference interval: 5.5–11.0 × $10^9/ℓ$) compared with previous findings of 6.64 × $10^9/ℓ$[26]; and lymphocytes with a value of 5.53 × $10^9/ℓ$ (reference interval: 4.0–6.3 × $10^9/ℓ$) compared with. 4.63 × $10^9/ℓ$[26]. The proportion of neutrophils at Day 1 was reduced to 0.92 × $10^9/ℓ$ (reference interval: 1.02–3.87 × $10^9/ℓ$) by comparison with 1.13 × $10^9/ℓ$[26]. There were Heinz bodies present on numerous RBC and there were many immature RBC (reticulocytes and immature forms).

Zinc and glucose concentrations on Day 1 were increased at 172.8 (sick) *vs.* 67 (healthy) µ g/100 mℓ and 4.2 g/ℓ (1.7 g/ℓ min.; 3.3 g/ℓ max.) *vs* 0 g/ℓ, respectively (Table 1). ALP concentrations in the sick rats were elevated at 133 UI/L (37 °C) (reference interval: 15–85 UI/ℓ) by comparison with a healthy value of 79 UI/ℓ of the rat in our study (Table 1). Hct at Day 1 was low at 31 % *vs* 40 % in the healthy rat (Table 1). Urine volume was elevated on Day 1 (Table 1). Results from Day 1 prompted, at the time, possible diagnoses of zinc toxicity, hyperglycaemia, or glucosuria as a consequence of renal damage.

Plasma zinc concentrations were elevated from Day 1 until the end of Week 7, thereafter reaching values that did not differ from the healthy values (Table 1). Following source removal, *i.e.* the zinc-coated cage, urinary glucose was attenuated to 1.7 g/ℓ at the end of Week 2 (Table 1). Urinary glucose concentrations progressively decreased over subsequent weeks reaching 0 g/ℓ at the end of Week 5 (Table 1). ALP was increased up to the end of Week 4 (Table 1). Hct remained attenuated up to the end of Week 3 (Table 1). Urine volume, although greater than healthy value, decreased steadily, reaching a value by the end of Week 7 that did not differ from the healthy value (Table 1).

DISCUSSION

Giant rats are one example of an exotic pet. They are less commonly kept that the domestic albino rat, principally due to lack of knowledge of this species amongst buyers and expense at purchase[8]. As such, although this clinical case appears due to a low-incidence toxicity, it is essential that it is reported for small animal veterinary knowledge. We deduced that the sick rat was suffering from a combination of zinc toxicity and stress-induced glucosuria. Poisoning from zinc was due to the rat's cage being made of galvanised steel on which it gnawed. Giant rats commonly knaw at their cages and inclusions therein; this behaviour is neither associated with explorative nor with supportative activity when climbing within the cage[8]. It may have been probable that the gnawing activity was a consequence of inadequate housing, but this was not investigated in the current study. It was noted that the rat in question was kept in isolation in its cage. It is possible that the glucosuria was a consequence of zinc toxicity resulting in renal damage. We suggested that chronic zinc exposure manifested itself sympathetically in muscle twitching possibly through stimulated release of neurotransmitters. Allied, albeit contradictory studies, have demonstrated that zinc stimulates spontaneous release at neuromuscular junctions[17,18,28] and inhibits the entry of calcium into nerve terminals thereby inhibiting transmitter release[27]. Plasma concentration of zinc in the healthy rat at Day 1 in this study lay within ranges reported in a previous study[21]. The sick rat had clearly consumed more that the recommended dietary allowance of 15 mg Zn/d in humans[12]. Species-specific pharmacokinetic properties of Zn in giant rats is unknown. Indeed, high Zn levels could be either due to high daily intake of Zn or accumulative effects of the ion. Icterus has been reported in cases of zinc intoxication in dogs[16,23]. The yellow mucus membranes characteristic of icterus may be a consequence of extra-vascular haemolysis. Microscopic analysis demonstrated the existence of Heinz bodies in RBC, a well-known side effect of zinc toxicity[16]. The presence of immature RBCs was indicative of regenerative anaemia. The anaemia, however, had not progressed into sideroblastic[4,30] or hypocupremia anaemia[30] suggesting a moderate exposure to zinc. Neutropaenia, as a result of zinc toxicosis, has been confirmed in previous investigations[4,21,35]. We suggest that zinc interferes with the development of formed neutrophils in bone marrow by disrupting metabolic reactions in committed stem cells. No evidence of infection was concluded as there was no left shift in or production of immature white blood cells.

Urinary excretion of zinc is increased in human patients with Type 1 diabetes mellitus[5]. It is probable that although there is a positive correlation of mean fasting plasma zinc, duration of diabetes and glucose excretion[11,31], the glucosuria observed in our study was not linked to the hyperzincaemia. Diabetes certainly elevates plasma ALP levels[24,33]. The normal range of ALP was in close agreement with studies in other animals[19,29]. The attenuated ALP levels from Day 1 to the end of Week 4 were commensurate with a declining urinary glucose concentration, suggesting transitory hyperglycaemia. We suggest that due to excessive stress, the sick rat developed transitory hyperglycaemia with glucose spilling into the urine resulting in the observed glucosuria. Indication of such has been described in other studies[15,34]. However, in the absence of blood glucose determinations, these deductions can only be considered specu-

lative. As these rats were not sacrificed due to expense, it was impractical to draw blood for glucose determinations as this may have adversely influence the health of the animals. Indeed, the 1 mℓ of blood drawn for haematological and biochemical analysis was insufficient for glucose determination.

The rat was anaemic as shown by the low haematocrit and its improvement following treatment. Although the source of zinc was removed by Week 2, the continuation of vitamin B_{12} and DTPA therapy was necessary to stimulate erythropoeisis in order to improve the anaemia[13] and remove the zinc[9]. Although the urine volume was elevated at Day 1 and the end of Week 2–6, it did not reach values critical enough to require intravenous fluid management. We further suggest that the protective effect of vitamin B_{12} in zinc toxicity is due to interference in body absorption of zinc through formation of readily excretable complexes[36].

In conclusion, zinc toxicity establishes systemic aberrations and is of clinical interest to exotic, small animal veterinarians as rodents frequently gnaw at their cages. Future work may investigate how long zinc remains in the gut after removal of source. Further experiments might be designed to investigate the cause of glucosuria via investigations on renal parameters. We suggest using the Sprague-Dawley model due to the expense and slow reproductive capacity of the giant rat. Other parameters measured to further confirm zinc toxicity may include: plasma copper concentrations; azotaemia; bilirubinaemia; pancreatic, hepatic and renal functionality; body temperature; and evidence of depression. Moreover, further investigations of environmental enrichment of the housing of African giant rats in pairs or more in order to alleviate the stresses of captive housing should be done. Studies have shown that stress responses in rats are reduced when they are housed in groups[14,22,32]. It is also essential that the zinc composition in the feed and water is determined, to ensure a balanced diet so avoiding the engaging of pica.

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