CASE REPORT

Severe Lead Toxicosis in a Lionhead Rabbit

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Abstract

Introduction Lead toxicosis occurs in veterinary patients, with few reports involving rabbits, and no previous reports using oral calcium disodium EDTA.

Case report A 7-year-old male castrated Lionhead rabbit presented to the Cornell University Hospital for Animals (CUHA) for evaluation after a 2-day history of lethargy and a 2-week history of hyporexia. The patient had been observed pulling paint from the walls of the home, a house built circa 1900, in the months prior to presentation. The patient was moderately anemic with a hematocrit of 21% with red blood cell morphological changes consistent with lead toxicosis, including basophilic stippling, nucleated red blood cells, and polychromasia. Radiographic images of the abdomen revealed excessive accumulation of gas in the gastrointestinal tract in a pattern consistent with gastric stasis and numerous small mineral to metallic opacities in the cecum. The blood lead concentration was 792 µg/dL, confirming the diagnosis of lead toxicosis with secondary gastrointestinal stasis. The rabbit was hospitalized for treatment with oral and

subcutaneous calcium disodium EDTA for 4 days and then discharged home to the care of the owners.

Discussion Severe lead toxicosis in a rabbit can be treated successfully with oral and subcutaneous calcium disodium EDTA and aggressive supportive treatment.

Keywords Lead · Rabbit · Ca₂Na₂EDTA · Gastric stasis

Introduction

Anecdotal reports of lead toxicosis in domestic rabbits are relatively common, but published reports are fewer [1–3]. The most common source of lead for rabbits and other companion animals is lead paint, which is still present in homes older than 1972 [1, 4, 5].

The most commonly reported clinical sign of lead toxicosis in rabbits is hyporexia, though neurological signs including torticollis, seizures, hind limb ataxia, tremors, depression, and blindness, as well as behavioral changes have been reported [5, 6]. Changes on physical examination can include thin body condition, cardiac arrhythmias, neurological abnormalities, hypertension, and pale mucous membranes [6]. A case report of two dwarf rabbits with lethal lead toxicosis described hepatic, renal tubular, and cardiac necrosis at necropsy, indicating that clinical signs were related to the extent and degree of organ injury [2].

History of exposure, clinical signs, anemia, finding nucleated red blood cells and reticulocytes on blood smears, and presence of lead in the blood support the diagnosis of lead poisoning [7]. Lead is not a required nutrient, has no known biological function, and can cause adverse effects at very low concentrations; however, rabbits with no apparent clinical signs of poisoning have been reported with blood lead concentrations up to 27 µg/dL [3]. A blood lead concentration of

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approximately 80 $\mu\text{g}/\text{dL}$ was associated with clinical pathological changes such as mild anemia, poikilocytes, basophilic stippling of red blood cells, hypochromic erythrocytes, target cells, lymphocytosis, neutropenia, and eosinopenia [3]. Anorexia has been reported in rabbits with blood lead concentrations of 140 $\mu\text{g}/\text{dL}$ [3]. Anorexia, neurologic signs, and fatality were reported in a rabbit with a blood lead value of 360 $\mu\text{g}/\text{dL}$ [2]. Treatment is usually initiated in companion animals (usually dogs and cats) with blood lead concentrations ≥ 30 $\mu\text{g}/\text{dL}$ [3].

The most commonly reported treatment for rabbits with lead toxicosis is supportive care and serial abdominal radiographs to assure that the ingested lead passes through the gastrointestinal tract, followed by chelation with 27.5 mg/kg calcium disodium EDTA administered subcutaneously every 6–12 h for 2–5 days [6, 8]. Multiple courses of treatment are sometimes necessary, and a 5–7-day break between each round is recommended [6]. Oral dosing of calcium disodium EDTA has not been reported in rabbits.

Case Report

History

A 7-year-old male castrated Lionhead rabbit was presented to Cornell University Hospital for Animals (CUHA) for evaluation of anorexia, lethargy, and decreased number and size of fecal pellets.

Discussion with the client revealed that the patient was fed a diet of commercial rabbit pellets and a variety of grass hays offered free choice, with the addition of one to two baby-cut carrots daily. Fresh tap water was provided in a bottle. The patient had free and unsupervised access to the house during the day and was kept in a commercial wire cage at night. The cage was bedded with blankets and had a litter pan. The house, originally built in the early 1900s, was undergoing renovations over several months duration. Since the start of renovations, the rabbit had been observed peeling paint from the walls of the house.

Clinical Findings

On examination, the patient was quiet but alert and responsive. Dehydration was estimated to be approximately 5–7% based on a prolonged skin tent and slightly tacky mucous membranes. The mucous membranes were pale pink with a mildly prolonged capillary refill time of 2 s. The rabbit was in thin body condition with a body weight of 1.8 kg. The rectal temperature was 99.7 °F (reference interval = 101–104 °F) [7]. The hair coat was slightly rough. The rabbit had a heart rate of 240 beats per minute (reference interval = 103–325 beats/min) and was tachypneic with a respiratory rate of 200

breaths per minute (reference interval = 30–60 breaths/min) [7]. No cardiac murmurs or arrhythmias or adventitious lung sounds were detected on thoracic auscultation. On abdominal palpation, the cranial abdomen had a doughy consistency. Markedly decreased borborygmi were noted on abdominal auscultation. Bruxism, a sign of pain in rabbits, [7] was noted frequently throughout the exam. Other physical exam findings were within normal limits.

Blood samples were submitted for a complete blood count, plasma biochemistry panel, and a blood lead concentration. Two-view radiographs of the abdomen were taken, and images revealed a moderately distended stomach containing mixed fluid and gas opacity (Fig. 1). A round soft tissue opacity was noted near the pylorus surrounded by a gas cap, consistent with gastrointestinal stasis in this species [9]. The cecum contained numerous very small mineral or metallic opacities.

The results of the patient's complete blood count showed anemia with a hematocrit of 21% (reference interval = 36–48% [7]) and significant morphological changes to the red blood cells, including hypochromasia, nucleated red blood cells, keratocytes, schistocytes, and basophilic stippling (Fig. 2). The plasma biochemistry results showed changes consistent with mild dehydration (mild elevation in urea nitrogen and creatinine).

Whole blood in EDTA was analyzed for lead via graphite furnace atomic absorption spectroscopy. The patient had a

Fig. 1 Dorsoventral radiograph of the patient with suspected lead toxicosis; significant findings included a gas cap surrounding ingesta in the stomach and tiny mineral opacities in the lumen of the stomach and cecum

Fig. 2 Red blood cell abnormalities in this patient were consistent with lead toxicosis, including the presence of nucleated red blood cells (*large arrows*), basophilic stippling (*small arrows*), and polychromasia (image courtesy Laura E Brandt)

blood lead concentration of 792 $\mu\text{g}/\text{dL}$. Blood lead concentrations of 30 $\mu\text{g}/\text{dL}$ or greater indicate significant exposure and support a diagnosis of lead toxicosis when clinical signs are present [10]. Due to the patient's clinical signs of anorexia and chronic weight loss, the hemogram results, the radiographic findings, and the markedly elevated blood lead concentration, a diagnosis of lead toxicosis was made.

Prognosis, Treatment, and Outcome

The patient was given a poor prognosis. The rabbit was treated with 25 mg/kg calcium disodium EDTA administered subcutaneously every 8 h, as recommended for rabbits and other small animals [8]. Because the suspected source of lead remained in the gastrointestinal tract, calcium disodium EDTA was also administered orally at a dose of 25 mg/kg every 8 h in the hopes of preventing absorption.

The patient's gastrointestinal stasis was treated with cisapride (0.5 mg/kg by mouth every 12 h [8]), syringe-feeding a critical care formula (Oxbow Animal Health brand Herbivore Critical Care Diet administered at 15–20 mL/kg every 8 h), and subcutaneous fluid administration (35 mL/kg every 8 h). Other supportive treatments included pain management with buprenorphine (0.05 mg/kg subcutaneously every 8 h [8]) and gastroprotectant treatment with sucralfate (25 mg/kg by mouth every 8 h [8]) and famotidine (0.5 mg/kg by mouth every 12 h [11]).

The patient was slightly brighter on the third day of treatment and was observed eating small amounts of food. The hematocrit increased by approximately 1% each day of hospitalization to 25% at discharge 4 days after admission.

Chelation therapy was continued at home for a total of 14 days. Other treatments initiated at CUHA were continued,

with the exception of buprenorphine. Instead, tramadol was given at a dose of 5 mg/kg by mouth every 8 h for pain control. The owner was instructed to prevent access to the painted walls that the rabbit had been chewing on. The patient's hematocrit was rechecked 2 weeks after the initial visit and reported to be 33%, and the patient was eating normally, gaining weight, and appeared bright and alert. The patient was then lost to follow-up.

Discussion

This report describes a case of severe lead toxicosis in a domestic rabbit successfully treated with chelation therapy and supportive care. In many species, the hallmark signs of lead toxicosis are gastrointestinal and neurological signs [2, 10]. This patient did not have any clinical signs other than decreased appetite and lethargy.

It is important to note that in this severely affected rabbit, the clinical signs were relatively mild and vague. This was consistent with previous case reports documenting seven patients total in which all rabbits were presented for inappetence. In addition, one rabbit had muffled heart sounds and tachypnea due to pleural effusion [3], four had hind limb ataxia, three had tremors, and one had hematuria [1–3]. Because of the nonspecific nature of these signs, a careful history, physical exam, hematocrit, and blood smear evaluation should be included in the diagnostic plan for rabbits presenting with anorexia. Whole blood, not serum or plasma, needs to be submitted for blood lead concentration analysis because at least 90% of circulating lead is bound to red blood cells in circulation [7]. Prompt diagnosis is important not only for rapid initiation of treatment, but also because lead is an environmental contaminant and house pets can act as sentinels to lead contamination within a home [1, 4, 5, 10].

In the patient described in this report, there were several mineral foreign bodies present in the patient's stomach and cecum as indicated by the radiographic images. This finding was also a feature of previous reports of lead toxicosis in rabbits [2, 3]. This, in addition to a thorough history, placed lead as a top differential diagnosis in these cases. In all cases, lead toxicosis was confirmed by elevations in the blood lead concentrations of the rabbits, which ranged from 40 to 360 $\mu\text{g}/\text{dL}$, compared to 792 $\mu\text{g}/\text{dL}$ in this rabbit case [1–3]. Based on these few reports, reported blood lead concentration could not be correlated with severity of clinical signs. This observation is consistent with lead toxicosis in other species, such as humans and dogs, in which there is often variability in severity of clinical signs at a similar blood lead concentration [1, 4, 12]. This can be attributed both to individual variability [12] and the relatively short half-life of lead in blood (35 days) and its deposition in other tissues, making blood lead

concentration an unreliable representation of the severity of chronic exposure [13].

Although not validated in rabbits, the most commonly recommended treatment protocol for lead toxicosis is 5 consecutive days of treatment with subcutaneous calcium disodium EDTA every 6 h, followed by 5–7 days of no treatment, with a second 5-day course given if necessary [6]. Calcium disodium EDTA can have adverse effects, including nephrotoxicity and the binding of essential minerals such as zinc, iron, calcium, and copper [10].

Although not reported previously in rabbits, calcium disodium EDTA was administered orally in this patient at a dose of 25 mg/kg every 8 h as well as subcutaneously with the intention of binding the lead presumed to be present in the gastrointestinal tract. The patient was treated for 14 consecutive days with both subcutaneous and oral calcium disodium EDTA rather than the recommended 5 due to the remarkably high blood lead concentration. Based on clinical improvement, calcium disodium EDTA treatment was not repeated.

Removal of lead from the gastrointestinal tract is recommended before treatment with calcium disodium EDTA because chelation can increase gastrointestinal absorption [14]. Two previous case reports describe the use of lubricants and laxatives and delaying treatment with calcium disodium EDTA until no lead was apparent in the gastrointestinal tract on radiographs [3]. However, in this patient, treatment was initiated immediately due to the severity of the toxicosis. The invasiveness and risks associated with surgical decontamination of the cecum, especially in the face of gastrointestinal stasis, were also considered in the decision to commence treatment with lead present in the gastrointestinal tract. Unfortunately, serial radiographs were not taken of the patient to determine clearance of lead from the gastrointestinal tract.

Parameters monitored during therapy in this patient included the patient's hematocrit, weight, and resolution of clinical signs.

Three rabbits with neurological signs in one of the previous case reports died, one before the initiation of chelation and one after four treatments with calcium disodium EDTA (blood lead concentration 360 µg/dL) [1, 2]. The rabbits in the other case report, one of which had pleural effusion (blood lead concentration 70 µg/dL) and one of which presented with anorexia only (blood lead concentration 40 µg/dL), survived after lead removal with lubricant/laxatives and subcutaneous calcium disodium EDTA administered every 6 h for 5 days [3]. Even though the patient in this report was lost to long-term follow-up, he continued to improve during the course of therapy.

Conclusion

Veterinary patients with markedly elevated blood lead concentrations can be successfully managed with supportive care and immediate and aggressive oral and subcutaneous chelation with calcium disodium EDTA.

Compliance with Ethical Standards

Conflicts of Interest None

Sources of Funding None

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