2023, Scienceline Publication
World's Veterinary Journal
World Vet J, 13(4): 626-629, December 25, 2023
ISSN 2322-4568

DOI: https://dx.doi.org/10.54203/scil.2023.wvj67

A Pathologic Case of Gout Tophi Deposition with a Concurrent Systemic Bacterial Infection in a Leopard Gecko (*Eublepharis macularius*)

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CASE REPORT
pii: S232245682300067-13
Received: 26 September 2023
Accepted: 15 November 2023

ABSTRACT

Gout is caused by excessive uric acid in the blood deposited in tissues (visceral gout) or joints (articular gout), leading to severe inflammation and pain. A female leopard gecko was presented to the University Veterinary Hospital, University of Putra, Malaysia, with a history of swelling at the left caudal mandible, inappetence, and weight loss. An oral examination indicated a swollen mouth with scabs on the upper right mandible and multiple whitish deposits inside the mouth. The preliminary diagnosis was mouth rot, and the treatment included metronidazole and a multivitamin supplement. The leopard gecko died 12 days after treatment since there was no improvement. Post-mortem examination revealed that the liver was slightly enlarged with generalized moderate congestion and the presence of whitish deposits, as well as noticeable whitish deposits on the pleural surface of the lungs. Histopathological examination of the lungs revealed a granuloma with an inflammatory reaction predominantly by abundant mononuclear cells and fibrin deposition. An irregular collection of amorphous materials in the visceral pleura suggested gout tophi. The liver was infiltrated with amorphous material and fibrinous tissue, and it had mild congestion, indicating visceral gout and bacterial infection. *Klebsiella pneumoniae* and *Proteus mirabilis* were isolated from the lungs and liver samples, respectively. In conclusion, gout tophi is common in reptiles, but visceral involvement is rare, and early detection is critical to avoid secondary bacterial infection, as demonstrated in this case.

Keywords: Amorphous material, Bacterial infection, Gout tophi, Histopathology, Leopard gecko

INTRODUCTION

Leopard geckos belong to the *Eublepharidae* family, which has six genera and 38 species worldwide (Uetz et al., 2023). Leopard gecko, a popular exotic pet, can live up to 22 years and are native to central and south Asia, including Afghanistan, Iraq, Iran, Pakistan, and India (Woods, 2001). In the wild, they eat invertebrates, but in captivity, they eat a variety of invertebrates, such as crickets, worms, and locusts (RSPCA, 2019). The ability to manage uric acids is determined by the amount of protein consumed, the type and frequency of feeding, and the state of hydration in all reptiles, including geckos (Rich and Axelson, 2023).

Gout is a metabolic disorder resulting from either the overproduction of uric acid or the body's inability to eliminate it, leading to excessive amounts of uric acid in the blood, which eventually deposited in tissues (visceral gout) or joints (articular gout), resulting in severe pain and inflammation (Lock, 2017; Doneley et al., 2018). High-protein diets, dehydration, low temperatures, hunger, nephrotoxic substances, and inactivity are possible risk factors (Mader, 2005; Rich and Axelson, 2023).

Several clinical signs of gout have been reported in various species of reptiles. Lethargy, weakness, painful joints, and swollen feet are symptoms of articular gout (Mader, 2005; Lock, 2017). In visceral gout, a swollen mouth due to stomatitis can be misdiagnosed as infectious stomatitis in snakes, in which the whitish lesions in the gingiva were thought to progress from the infectious stomatitis, as it were the depositions of gout tophi and anorexia (Mader, 2005). The present study reported pathological findings of gout tophi in a pet leopard gecko in Malaysia.

CASE REPORT

A one-year-old female leopard gecko weighing 35 gm was presented to the Avian and Exotic Animal Unit, University Veterinary Hospital UPM, with complaints of weight loss and a swollen mouth. The leopard gecko was the only one in a

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vivarium with moist and warm hiding places. It was occasionally fed mealworms with calcium powder and had a drinking water source available 24 hours a day. As mentioned by the owner, no abnormalities were observed during the most recent shedding. The gecko began to eat less and gradually lost tail thickness, as well as developing left-side mouth swelling. Physical examination revealed that the gecko was quiet but alert and responsive, with a lower body condition score assessed by the amount of fat storage in the tail (Figure 1A). It had a swollen mouth at the left caudal mandibular area (Figure 1B) with scabs visible on the upper right side, multiple whitish deposits inside the mouth when opened, and retained shed skin on the toe. At this point, a preliminary diagnosis of stomatitis was made. The prescribed treatment plan included oral administration of metronidazole (Metrogyl® suspension, Unique Pharmaceutical Laboratories, India) at a dosage of 30 mg/kg every 48 hours for two treatments. Additionally, 1 mL of multivitamins (Uphavit syrup, Duopharma, Malaysia) was prescribed daily until recovery. In addition, it was advised to increase the humidity from 20% to 40% and monitor the vivarium using a hygrometer.

However, 12 days post-treatment, the gecko was found dead and was immediately sent to the Post-mortem Laboratory, Veterinary Laboratory Service Unit (VLSU), Faculty of Veterinary Medicine, Universiti Putra Malaysia, for further investigation. The post-mortem examination revealed that the carcass was in fair condition, with minimal visceral and subcutaneous fat stores, incomplete skin shedding and sunken eyes indicating severe dehydration. The liver was slightly enlarged with generalized moderate congestion, and whitish deposits were also present on the pleural surface of the lungs. Histopathological findings by hematoxylin-eosin (H&E) staining of the lungs included dilated capillaries in the alveolar walls, thickened alveolar walls and moderate vascular congestion with a morphological diagnosis of bacterial infection, lung granuloma with inflammatory reaction predominantly by abundant mononuclear cells and fibrin deposition, apart from the presence of irregular accumulation of amorphous materials (gout tophi) in the lungs suggestive of bacterial infection and visceral gout, respectively (Figure 2 A-C). The visceral pleura was covered by abundant fibrin, necrotic cellular debris, and it was expanded by increased amounts of fibrous connective tissue and the infiltration of amorphous materials, indicating bacterial infection and visceral gout, respectively (Figure 2B). The liver was moderately congested with degenerating hepatocytes containing numerous cytoplasmic lipid droplets, and the infiltration of amorphous materials and fibrinous tissue is suggestive of bacterial infection and visceral gout (Figure 2C). Bacterial culture of the lungs and liver samples revealed *Klebsiella pneumonia* and *Proteus mirabilis* were isolated with degrees of bacteria isolation of 2+ and 4+, respectively. Based on the findings, the final diagnosis was visceral gout with a systemic bacterial infection.

DISCUSSION

Gout can be caused by uric acid overproduction, such as long-term dehydration and a high-protein diet, or by a failure to excrete uric acids due to renal failure (Lock, 2017). Environmental changes, particularly temperature and humidity, may disrupt reptiles' physiological functions and homeostasis, deteriorate their general health, and cause dehydration. In this case, the gecko refused to eat for more than 2 weeks, while force-feeding, including the water, was deemed crucial. Improper care may result in dehydration. A high-protein diet may increase the chances of hyperuricemia (Hong et al., 2020). According to Liu et al. (2020), mealworms have approximately 17.6% protein and 49.1% dry matter, so regular consumption of mealworms may contribute significantly to the high uric acid production. Some of the clinical symptoms associated with visceral gout in reptiles, including depression, weakness, and dehydration, as well as reluctance to move and eat, were noted in this gecko (Lock, 2017). In cases of articular gout, swollen joints in the legs and feet can be seen, along with or without nodules on the ribs, but this was not the case in this instance. In leopard geckos, hyperuricemia is defined as uric acid levels greater than 8 mg/L (Mader, 2005). A radiograph is another diagnostic test that is less invasive than blood collection and can be used to diagnose gout in reptiles and leopard geckos (Lock, 2017).

There is little research on the treatment of gout in reptiles. According to Martinez-Silvestre (1997), allopurinol therapy at the dosage of 20 mg/kg is effective in treating tortoises with gout. Allopurinol dosages are based on human prescription, and while they have no side effects, they should be used cautiously in reptiles. In that study, 97.3% of tortoises were given 50 mg/kg orally once a day for 30 days, leading to reduced uric acid by day 7 post-treatment. Furthermore, the medication was continued for 3 years, and administered once every 3 days. The urate tophi disappeared 2 to 4 months after treatment with concentrations less than 2 mg/L of uric acid. Thus, the use of allopurinol for the treatment of gout in all reptile species should be investigated further. Allopurinol works by inhibiting the actions of xanthine oxidase to promote urate excretion and manage acute gouty arthritis attacks with anti-inflammatory drugs such as colchicine and corticosteroids (Mader, 2005).

In this case, the main cause of visceral gout would be dehydration due to low humidity, which impaired the kidney's ability to remove uric acid properly, causing uric acid to accumulate in the blood and cause hyperuricemia (Mader, 2005; Boyer et al., 2014). This caused uric acid crystallization, leading to deposits in internal tissues and histopathologically observed in the visceral pleura, lungs, and liver, as seen in this case. The likely pathogenesis for this case included injury to the mouth, leading to the loss of the skin barrier. Subsequently, this loss facilitated the

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development of stomatitis (mouth rot) by opportunistic pathogens of the normal flora from the oral cavity. The resulting pain further contributed to reduced feed and water intake, resulting in dehydration. Next, the leopard gecko became uncomfortable eating or drinking, resulting in inappetence and dehydration, and consequently, problems, such as dysecdysis arose. The cause of death for the gecko could be attributed to circulatory failure resulting from a decrease in cardiac output caused by a decrease in venous return. This decline can be a consequence of vasodilation caused by bacteremia or septicemia from the proliferation of bacteria in the lung. Concurrently, there was bacterial proliferation in the lungs, along with the presence of visceral gout due to hyperuricemia. The hyperuricemia could have resulted from the invasion of pathogenic bacteria through the respiratory tract from the oral cavity either through ingestion or ascending infection of stomatitis (mouth rot) caused by opportunistic pathogens of the normal flora, such as *Proteus mirabilis* and *Klebsiella pneumonia*. *Proteus mirabilis* and *Klebsiella pneumonia* are classified as normal flora in many reptiles (Gigani et al., 1986; Ghosh et al., 2018). The presence of these bacteria in the studied tissues indicated bacteremia or septicemia, originating from the normal flora becoming opportunistic pathogens.

CONCLUSION

Visceral gout can be misdiagnosed since such an occurrence is rare in leopard geckos, compared to articular gout. The prognosis is poor with secondary bacterial infection. A proper diagnosis is required to determine the definitive diagnosis and formulate effective treatment.

DECLARATIONS

Acknowledgments

The authors are thankful to all staff at the Post-mortem and Bacteriology Laboratory, Faculty of Veterinary Medicine, University of Putra, Malaysia.

Funding

The study received no financial assistance.

Authors' contribution

Mazlina Mazlan, Muhamad Alif Zakaria, and Mohd Asrul Syafiq performed the necropsy and diagnosis. Mohd Asrul Syafiq, Mazlina Mazlan, Luqman Abdul Samad, and Azlan Che-Amat contributed to the case analysis and drafted a manuscript. Azlan Che-Amat and Mazlina Mazlan revised the final edition of the manuscript. All authors approved the article before publication in the present journal.

Competing interests

There is no conflict of interest.

Ethical consideration

The owner of the gecko has given consent and signed the permission for data publication. The authors have checked and compiled ethical issues (including plagiarism, consent to publish, misconduct, data fabrication and/or falsification, double publication and/or submission, and redundancy).

Availability of data and materials

The data of the current case report are available.

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