Please Note: This Case Summary was submitted in 2024, when a Discussion section was not required. All 2025 case summary submissions MUST include a Discussion section.

Cutaneous Mast Cell Tumor in a Domestic Ferret (*Mustela putorius furo*).

Introduction

Cutaneous and subcutaneous neoplasia are common in the domestic ferret (*Mustela putorius furo*). Up to 20% of reported neoplasms in ferrets originate from those locations. Two of the most common cutaneous neoplasia in ferrets are mast cell tumors and basal cell tumors[1].

Mast cells are derived from bone marrow. Unlike other hematopoietic cells, they leave the bone marrow as a precursor cell and only mature upon entering the various tissue types, such as connective tissue or mucosa[2]. Mast cells mediate inflammation by releasing chemicals like histamine and cytokines by degranulation upon cross-linking immunoglobulin E receptors.

Cutaneous mast cell tumors (cMCT) are a common neoplasm reported in most mammalian, avian, and reptile species. cMCT originate from the mesenchymal tryptase containing mast cells[2]. While the oncogenesis of cMCT in the ferret is unknown, in canine cMCT the mutation of the c-KIT gene, a gene for the KIT tyrosine kinase receptor, appears to play a critical role. Specific mutations in the c-KIT gene are correlated with the aggressive behavior of canine cMCT. The KIT receptor can be expressed in one of three ways: 1 the mast cells express KIT mainly on the cell membrane; 2 the mast cells express KIT in the cytoplasm primarily adjacent to the nucleus; 3 the mast cells express KIT diffusely throughout the cytoplasm[2]. In canine, KIT expression patterns 2 and 3 are associated with aggressive behavior of the neoplasm[2]. However, this does not appear to be correlated in ferrets, where they exhibit patterns 1 and 3 with no correlation to the behavior of the neoplasm[3].

cMCT are considered benign in ferrets, with no reported distant metastasis[1,3,4]. Macroscopically, they appear as a discrete neoplasm often described as 1-4 mm in diameter, round, plaque-like, with surface crusting appearing on the head, trunk, and extremities[1,3]. Alopecia on the ferret cMCT was only reported to be observed in about 10% of animals[3]. Ferret cMCT can be a single lesion or multiple discrete lesions[3]. There is variable pruritus associated with the cMCT. Two studies suggest that males may be more predisposed to cMCT[1,3], but no statistics were used to examine this finding. Most studies of ferret cMCT find the median age is between 4 and 5 years, but the range could be between 2 and 9 years[1,3].

Cytologically, ferret cMCT are round cells with granules similar to other mammalian cMCT. The granules can be observed using toluidine blue (TB) and Wright-Geisma (WG) stains, but it has been reported that Romanowsky stains (e.g., Diff-Quik) have intermittently failed to stain the granules[3]. This intermittent failure can make it difficult to definitively diagnose the neoplasm in a clinical setting using cytology. Histologically, ferret cMCT are like other mammalian species. There is variable eosinophilic infiltration[1,3]. Various amounts of cytoplasmic, metachromatic granules have been observed on the ferret cMCT histology. One study showed a small amount of faintly staining granules[1]. Another study reported that cMCT granules failed to stain with hematoxylin and eosin (H&E) and TB on histology but stained with significant granulation on cytology[3]. Another report showed significant cytoplasmic metachromatic granules when stained

with TB[4]. Lack of granules staining in ferret cMCT does not indicate poor differentiation, unlike in canine cMCT, which carries a poor prognosis.

Diagnosis of the cMCT in ferrets can be performed by fine needle aspirate cytology or impression smear. However, a biopsy with histopathology of the neoplasm may be required.

Treatment/Management/Prognosis

Because cMCT in ferrets have not been reported to metastasize, the prognosis is generally good[1,3]. In most cases, the neoplasm remains small, causes rare clinical signs, and requires no treatment. However, in cases where the pruritus causes significant self-trauma, the lesion is large, or for cosmetic reasons, complete surgical removal of the cMCT is curative[1]. While some practitioners have reported that ferret cMCT can spontaneously regress[5], no published studies or case reports in the literature exist.

In neoplasms appearing on the extremities, surgical excisions are at increased risk of a skin defect too large for adequate closure. Three methods are proposed to address this defect: reduce or regress the neoplasm with chemotherapeutic agents, provide new tissue in grafts or vascularized flaps, or allow the defect to heal by second intention. Using bleomycin as the chemotherapeutic agent in an electrochemotherapy protocol has shown cMCT to regress in two ferrets[4].

Case History and Presentation

A three-year-old, neutered male domestic ferret presented for a mass. The ferret was adopted by its owners a day before the exam from a friend who couldn't afford medical care. Previous owners noticed the mass for only seven days. The ferret would chew on the mass frequently throughout the day. The old and current owners were applying hydrogen peroxide twice daily. The general husbandry of the ferret needed to be improved. The ferret was kept alone in a small 2-level wire cage (0.8 m long x 0.5 m wide x 0.6 m high). Twice daily, the ferret wandered throughout a room that was not ferret-proofed. The ferret was fed Iams Indoor Cat food.

The ferret’s physical exam was overall unremarkable. The ferret weighed 900 grams and was in good body condition. It was euthermic, euhydrated, eupneic, and had a normal sinus heart rate. A mass was present on the dorsal aspect of the left hindlimb (Figure 1). The mass was large (2 cm in diameter), red, raised, hairless, and plateaued with an irregular texture and ulceration. No other skin lesions were noted.

The differential diagnosis included cutaneous mast cell tumor, basal cell tumor, cutaneous hemangioma, squamous cell carcinoma, and squamous cell papilloma.

Case Management and Outcome:

A fine needle aspirate biopsy was performed. The ferret was distracted by an assistant feeding a canned wet food. The mass was biopsied using the woodpecker technique with a 22-gauge

needle. A 6 ml syringe filled with air was used to eject the biopsy onto a slide. Another slide was placed onto the sample slide, and with gentle pressure, it was spread throughout. This process was repeated to produce two slides. The first slide was stained using a common commercial Romanowsky stain[a]. Clusters of discrete round, mononuclear cells, twice the size of red blood cells, with mild anisocytosis were observed. No intracytoplasmic granules were evident. Few inflammatory cells were visible, and no bacteria were observed. The findings were suggestive of either a cMCT or a basal cell tumor. No photos of the cytology were taken. Because the mass was much larger than the average ferret cMCT and there was a lack of cytoplasmic granules on cytology, it was recommended that an incisional biopsy be performed.

The pet's biopsy was rescheduled for the next day as it was the last appointment. The owners were advised to stop using hydrogen peroxide and were educated on ferret husbandry. While no anaphylactic degranulation of cMCT in ferrets have been reported, they have been observed in other species. Therefore, the ferret was placed on the antihistamine diphenhydramine (1 mg/kg PO BID). The owners elected to pick up over-the-counter pediatric diphenhydramine (12.5 mg/5ml).

The ferret returned and was fasted for 2 hours. Butorphanol[b] (0.2 mg/kg IM) and midazolam[c] (0.1 mg/kg IM) were administered. The ferret became sedated in about 5 minutes but never became unconscious. The ferret was offered a ferret vitamin paste as a distraction. A ring block around the limb was placed proximal to the mass using lidocaine[d] (2 mg/kg SQ) mixed with bupivacaine[e] (2 mg/kg SQ). After 2 minutes, a 20-gauge needle was used to test the sensitivity of the limb. When no reaction to the needle was observed, the procedure continued. The mass was gently cleaned using interchanging scrubs of chlorhexidine scrub[f] and saline for three rounds. Three full-thickness biopsies were collected from the mass using a 4mm punch biopsy tool. Each biopsy site was closed with a single interrupted suture of 4-0 polydioxanone[g]. The biopsies were placed into a buffered 10% formalin. While the ferret was sedated, a complete blood count and biochemistry were collected from the cranial vena cava. The ferret was recovered in a kennel with a forced-air thermal support unit[h]. After approximately 2 hours, the pet had recovered from the sedation. The pet was discharged with meloxicam[i] (0.1 mg/kg PO SID for seven days) for analgesia. While no bacteria were observed on the in-clinic cytology, amoxicillin-clavulanic acid[j] (12.5 mg/kg PO BID for ten days) was used for empiric antibiosis due to the ulcerated lesion. The owners were instructed to continue diphenhydramine treatments until directed to stop.

The biopsy samples were submitted for histopathology to an anatomical pathologist[k] with considerable experience in ferret histopathology. The pathologist diagnosed it as a cutaneous mast cell tumor with acute ulcerative dermatitis (Table 1). The complete blood count (Table 2) and the biochemistry (Table 3) were unremarkable.

The owners reported continued self-trauma, including the removal of the sutures from the biopsy. At the 7-day follow-up exam, the mass had not changed. Due to this continued self-trauma and the size and location of the mass, a board-certified surgeon was consulted. The surgeon

recommended a complete surgical excision of the mass. The surgeon indicated that a reverse saphenous transpositional skin flap would be required due to the location and lack of suitable closure tissue. The procedure was planned at the surgeon's earliest appointment two weeks after the follow-up exam. In the meantime, the ferret was bandaged using a simple two-layer system: the first layer was a non-adherent dressing[l] wrapped by a layer of a flexible cohesive bandage[m]. The owners changed the bandage every two days to prevent self-trauma.

Five days before the surgery, the owners reported that the mass had suddenly disappeared. The mass scabbed up about one week prior, and the ferret stopped chewing on it. The owners brought the ferret in for a follow-up exam, and spontaneous regression of the mass was confirmed (Figure 2). Six months later, the mass was still absent at the ferret's vaccination exam, and the hair had regrown. An annual exam one year after the 6-month exam, the ferret still showed no clinical signs.

References

1. Kanfer S, Reavill DR. Cutaneous neoplasia in ferrets, rabbits, and guinea pigs. *Vet Clin North Am Exot Anim Pract*. 2013;16(3):579-598. doi:10.1016/j.cvex.2013.05.006

2. Kiupel M. Mast Cell Tumors. In: *Tumors in Domestic Animals*. John Wiley & Sons, Inc.; 2016:176-202. doi:10.1002/9781119181200.ch6

3. Vilalta L, Meléndez-Lazo A, Doria G, et al. Clinical, Cytological, Histological and Immunohistochemical Features of Cutaneous Mast Cell Tumours in Ferrets (Mustela putorius furo). *J Comp Pathol*. 2016;155(4):346-355. doi:10.1016/j.jcpa.2016.07.012

4. Racnik J, Svara T, Zadravec M, et al. Electrochemotherapy with Bleomycin of Different types of Cutaneous Tumours in a Ferret (Mustela Putorius Furo). *Radiol Oncol*. 2018;52(1):98-104. doi:10.1515/raon-2017-0057

5. Mehler SJ, Bennett RA. Surgical oncology of exotic animals. *Vet Clin North Am Exot Anim Pract*. 2004;7(3):783-805, vii - viii. doi:10.1016/j.cvex.2004.04.011

End-Notes

a. DipQuick, Jorgensen Laboratories, Loveland, CO
b. Butorphanol Tartrate Injection 10 mg/ml, Dechra Veterinary Products, Overland Park, NJ
c. Midazolam Injection USP 50 mg/10ml, Almaject, Morristown, NJ
d. Lidocaine Hydrochloride Injectable 2%, Clipper Distributing Company, St. Joseph, MO
e. Bupivacain HCl injection USP 250 mg/ 50ml, "Marcaine 0.5%", Hospira, Lake Forest, IL
f. Chlorhexidine Scrub, First Priority, Elgin, IL
g. PDS II, Ethicon, Guaynabo, PR
h. Bair Hugger Warming Unit, 3M Healthcare US Opco LLC, Maplewood, MN
i. Meloxicam 1.5 mg/ml Suspension, "Meloxidyl", Ceva Animal Health, Lenexa, KS
j. Amoxicillin 50 mg/ml and Clavulanic Acid 12.5 mg/ml, "Clavamox", Zoetis, Kalamazoo, MI
k. Zoo/Exotic Pathology Service, Carmichael, CA
l. Telfa Non-adherent Dressing, Covidien, Mansfield, MA
m. Coflex Vet, Andover Healthcare, Salisbury, MA

Lab Data / Imaging

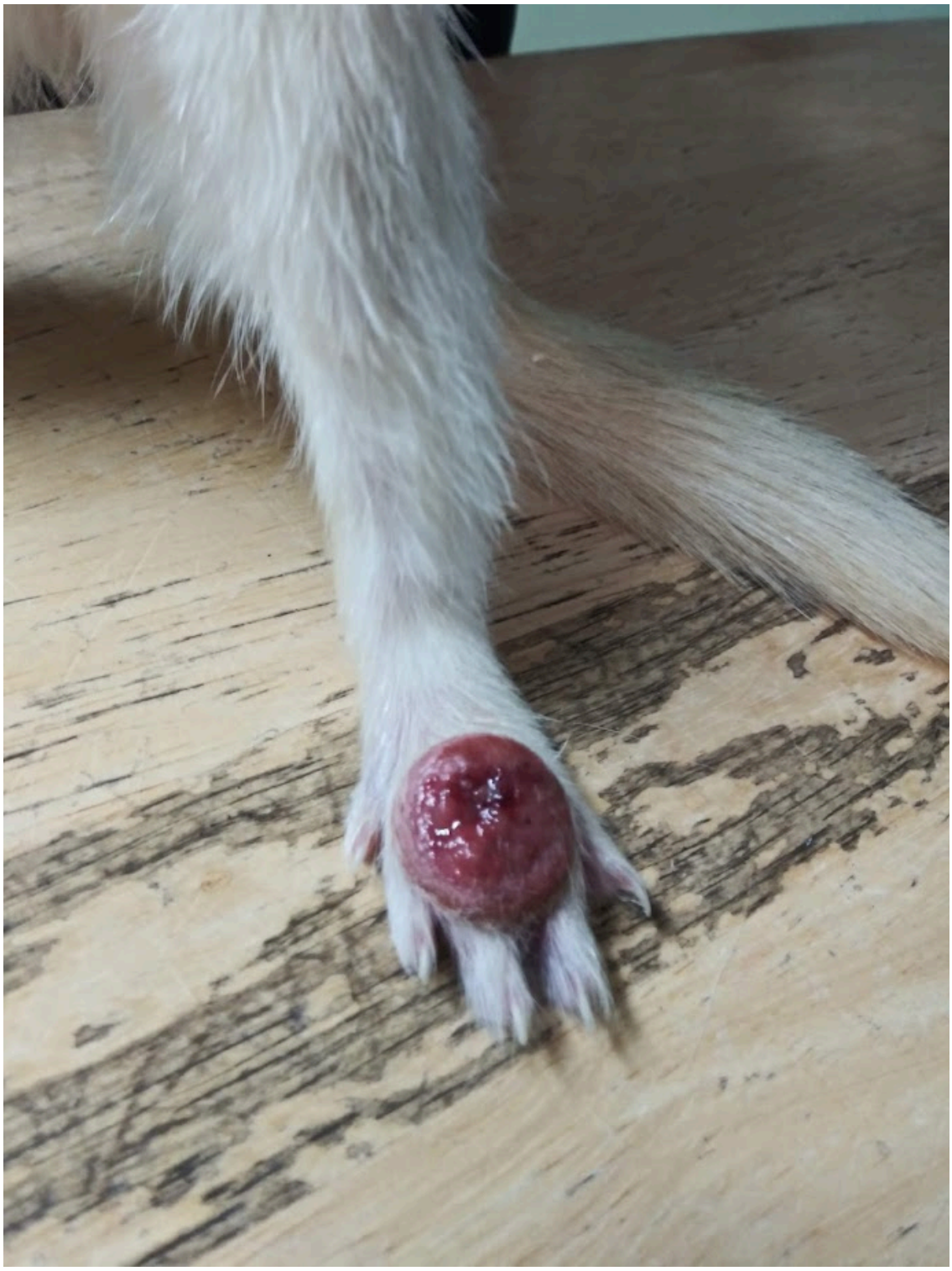

Figure 1. Mass on the dorsal aspect of the hindlimb.

Table 1. Histopathology report for a ferret with a cMCT.

Histopathology Report
MICROSCOPIC These are three 4-mm full-thickness biopsies. Multiple sections are examined. These biopsy sections are all similar and will be described as one. These are of haired skin. In these sections of skin, there are focal areas of ulceration and a serocellular inflammatory exudate adhered to the surface. There is some acute inflammation identified at the surface. The tumor itself extends from the dermal-epidermal junction through the deep tissues. These are of sheets of numerous closely placed round cells. These cells have moderate amounts of fine slightly granular amphophilic cytoplasm and an oval cell nucleus with a clumped chromatin pattern and indistinct basophilic nucleoli. The mitotic count is low at 1-2 per high-power field. There is some degeneration noted of the collagen bundles; however, the dermis is being effaced by this sheet of cells. An occasional eosinophil is admixed with these. DIAGNOSIS FOOT MASS: CUTANEOUS MAST CELL TUMOR AND ACUTE ULCERATIVE DERMATITIS COMMENT Cutaneous mast cell tumors are common skin tumors in ferrets. From our records, the incidence is equal between males and females and the average age is 4.5 years. The tumors most often appear as flat, alopecic, hyperkeratotic plaques that are variably pruritic. There is no site predilection. This mast cell tumor does not appear any more aggressive than typical mast cell tumors of ferrets; however, the location is unusual. I would wonder if the areas of ulcerative dermatitis are contributing to the severity of the lesion.

Table 2. Complete blood count for a ferret with cMCT. Normal reference intervals are provided by the reference laboratory.

Test	Laboratory Value	Normal Reference
White Blood Cell Count	4.4 K/µL	3.0-9.0 K/µL
Red Blood Cell Count	6.08 K/µL	4.5-9.5 K/µL
PCV	52 %	40-59%
Buffy Coat	0 %	0-0.5%
MCV	86 fl	
HGB	17.0 g/dL	13.5-18.0 g/dL
MCHC	32.7 g/dL	
Total Protein	6.5	5.0-7.0
Polychromasia	Normal	
Anisocytosis	Normal	
Neutrophils	2.948 K/µL	
Lymphocytes	1.144 K/µL	
Basophils	1.10 K/µL	
Eosinophils	0.88 K/µL	
Monocytes	0 K/µL	
Neutrophils	68%	43-84%
Lymphocytes	26%	25-65%
Basophils	2%	0-3%
Eosinophils	2%	0-5%
Monocytes	0	0-4%
Thrombocytes	Present	
Complete Cell Analysis: Red blood cells evaluated contain adequate mature hemoglobin content. Signs of heavy metal toxicity or other toxins are not found. Granulated white blood cells exhibit complete granular complement Mononuclear cells (lymphs, monos & azurophils) have cytoplasmic uniform color and consistency. Nuclei present are mature. In general, the		

peripheral blood appears to be in good condition.

Table 3. Serum biochemistry for a ferret with cMCT. Normal reference intervals are provided by the reference laboratory.

Test	Laboratory Value	Normal Reference
Calcium	9.9 mg/dL	8.0-10.0 mg/dL
Total Protein	6.5 g/dL	5.0-7.0 g/dL
Creatinine	0.4 mg/dL	0.4-0.7 mg/dL
Phosphorus	6.0 mg/dL	5.6-8.7 mg/dL
Albumin	3.2 g/dL	3.3-4.1 g/dL1
Globulin	3.3 g/dL	
A/G Ratio	0.97	
Glucose	111 mg/dL	100-207 mg/dL
BUN	24 mg/dL	10-45 mg/dL
Cholesterol	201 mg/dL	119-201 mg/dL
Total Bilirubin	<0.1 mg/dL	0.1-0.9 mg/dL
ALT	248 U/L	82-289 U/L
AST	123 IU/L	74-248 IU/L
Triglycerides	69 mg/dL	
Magnesium	2.0 mg/dL	

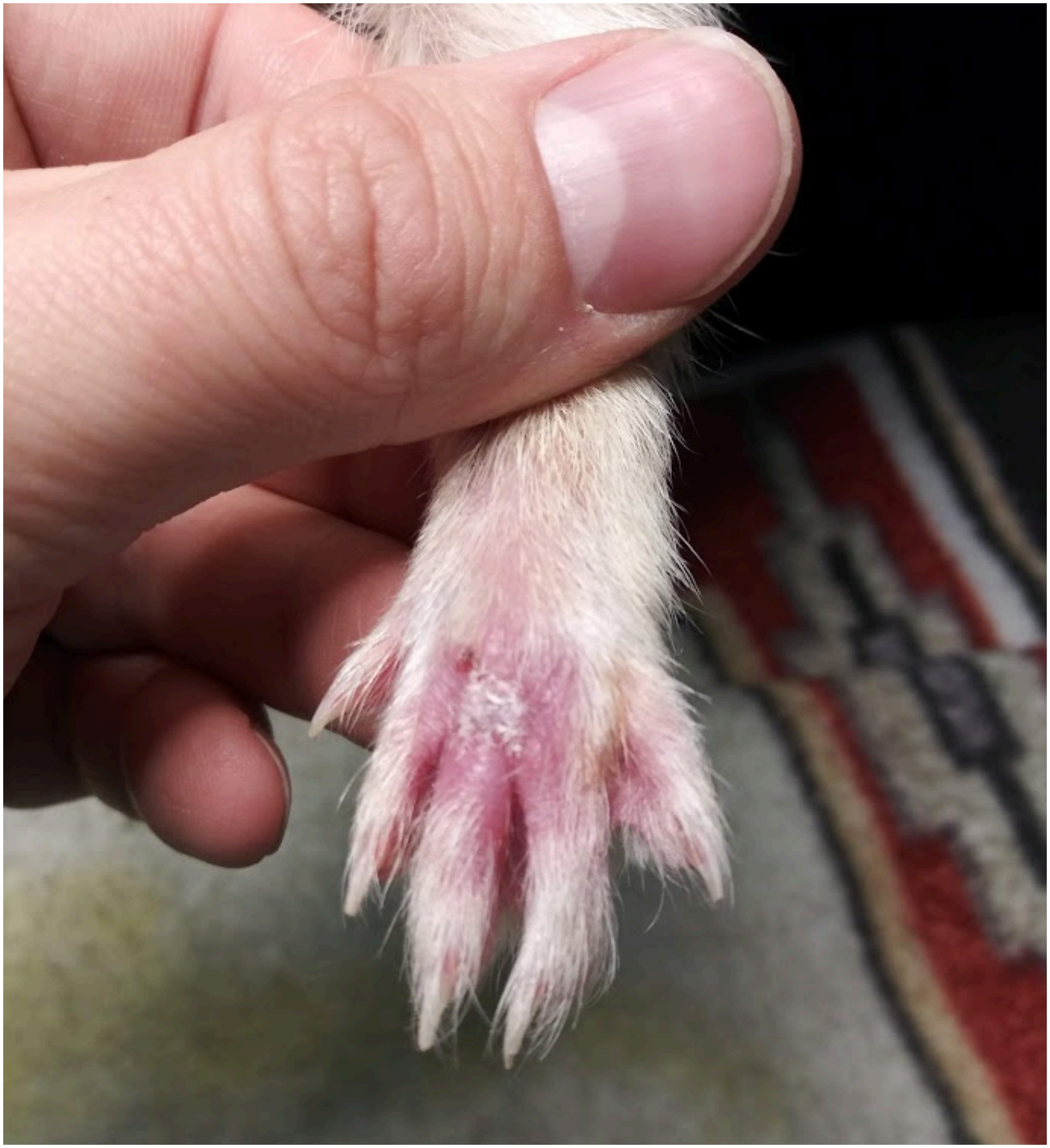

Figure 2. Hindlimb after mass spontaneously resolved.