

CASE REPORT

Foreign body reaction to ruptured follicular cysts in dogs

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Abstract

Background: Cutaneous cysts are common in dogs, and surgical resection is the recommended treatment. However, additional therapy may be required for ruptured follicular cysts with severe cutaneous complications.

Case presentation: A 3-year-old neutered male Samoyed was presented with multifocal masses on the forelimbs. A 5-year-old neutered female Maltese was also presented with multiple masses and ruptured lesions, which were ulcerative and painful, around the parotid and submandibular glands. The lesions were examined cytologically. In addition, bacterial and fungal cultures and histopathologic examination were performed. Cutaneous multifocal nodules in the Samoyed could not be diagnosed via cytological examination or bacterial/fungal culture. Histopathology revealed numerous follicular cysts with multiple pyogranulomas of various sizes, some of which contained central keratin debris. In the Maltese, cytologic examination revealed central keratins or enucleated ghost cells in the intact cysts and few keratinized squamous cells mixed with neutrophils, mucus and metachromatic cells in the ruptured cysts. Histopathologic examination revealed severely dilated follicular cysts. Oral steroid and cyclosporine therapy resulted in marked improvement in the aseptic pyogranulomas after 2 weeks in formal case and combined with a surgery for residual cysts in latter case.

Conclusions: We have reported two canine cases of ruptured follicular cysts causing foreign body-like aseptic pyogranulomas around cutaneous tissues and their successful management with pharmacological therapy and surgery.

KEYWORDS

dog, follicular cysts, keratin, pyogranuloma, rupture

1 | BACKGROUND

Cutaneous cysts associated with non-neoplastic and non-inflammatory lesions are common in dogs (Miller et al., 2013). Most cutaneous cysts in dogs and cats are of follicular epithelium origin and are further categorized according to the level of follicular origin (Gross et al., 2006). Follicular cysts usually present as solitary, firm and intradermal

nodules, and occasionally, as subcutaneous nodules (Gross et al., 2006). Occasionally, multiple cysts may occur and be associated with environmental or traumatic pressure in large dog breeds (Gross et al., 2006; Scott & Teixeira Edurado, 1995). Lesions may remain stable or progressively enlarge over time. Cutaneous cysts are often painful when associated with an inflammatory response. Secondary chronic frictional trauma may lead to obstruction of the follicular ostia (Gross et al., 2006).

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Single or multiple dermal/subcutaneous nodules should be differentiated from abscesses, cysts, papillomas, infections, neoplasms and lesions of immune-mediated diseases (Gross et al., 2006; Miller et al., 2013). Fine-needle aspiration cytology may be insufficient for accurate diagnosis, and therefore, biopsy is recommended. Cytological examination occasionally reveals a non-diagnostic appearance and inflammation secondary to infection. Treatment of asymptomatic intact follicular cysts may be deferred or surgical removal may be recommended in cases of pain; however, the procedure may be challenging due to the risk of ruptured lesions. A few reports describe the specific clinical outcome. Herein, we report two cases of foreign body reactions induced by ruptured follicular cysts in dogs and their successful management.

2 | CASE PRESENTATION

2.1 | Case 1

A 3-year-old neutered male Samoyed was presented with multifocal masses involving the forelimbs: two on the dorsum of the metacarpals and two on the dorsum of the olecranon of each forelimb (Figure 1a and b). The dog, which lived outdoors, showed signs of pain at the site of the lesions and often licked them. The lesions grew gradually. They were erythematous, firm and measured 2–4 cm.

The dog was alert and did not show any systemic symptoms. Results of haematological investigations were within the normal range, and fine-needle aspiration cytology of the lesions was non-diagnostic. Results of bacterial and fungal cultures were negative. Histopathologic examination of excisional biopsied skin samples showed multiple dilated hair follicles lined by squamous epithelium with a clear granular cell layer and a central lamellar layer of flaky keratins (Figure 1c) or a sparse or absent granular cell layer and

central pale, more amorphous keratins. These findings indicated the presence of multiple infundibular and isthmus-catagen cysts such as hybrid cysts. Multiple pyogranulomas composed of macrophages, giant cells and neutrophils were observed, some of which contained central keratin debris (Figure 1d). A case of pyogranulomatous dermatitis induced by ruptured follicular cysts was diagnosed.

The presence of multiple nodules and difficult access to the anatomic locations necessary for surgery made us worry about surgical intervention. Therefore, we tried to apply a medical treatment first. We planned to consider surgery if the lesion was not responsive to medical therapy. The initial treatment consisted of administration of oral steroids (prednisolone, 0.5 mg/kg, PO, bid; LLOYD Inc., Shenandoah, USA) and cyclosporine (5 mg/kg, PO, bid; Novartis, Basel, Switzerland).

After 2 weeks of treatment, significant improvement was observed in the lesions (Figure 1c and d), including reduced swelling and no signs of pain in the forelimbs. Dosage of the steroid was tapered gradually, and cyclosporine was continued for 2 months. The dog was referred to a local hospital for tapering the dose of cyclosporine at the owner's request. The dog had no relapse at the 6-month follow-up.

2.2 | Case 2

A 5-year-old spayed female Maltese was presented at the hospital with multiple cutaneous masses around the right ear. Some masses had ruptured and showed severe crusted lesions with bloody discharge. The dog had a 3-month history of lack of appetite and weight loss due to pain.

The masses were firm and circumscribed, and were located around the parotid and submandibular salivary glands (Figure 2a). After removing the crust and wiping the ruptured lesion, multiple holes with duct blockage were observed (Figure 2b). Secondary scant

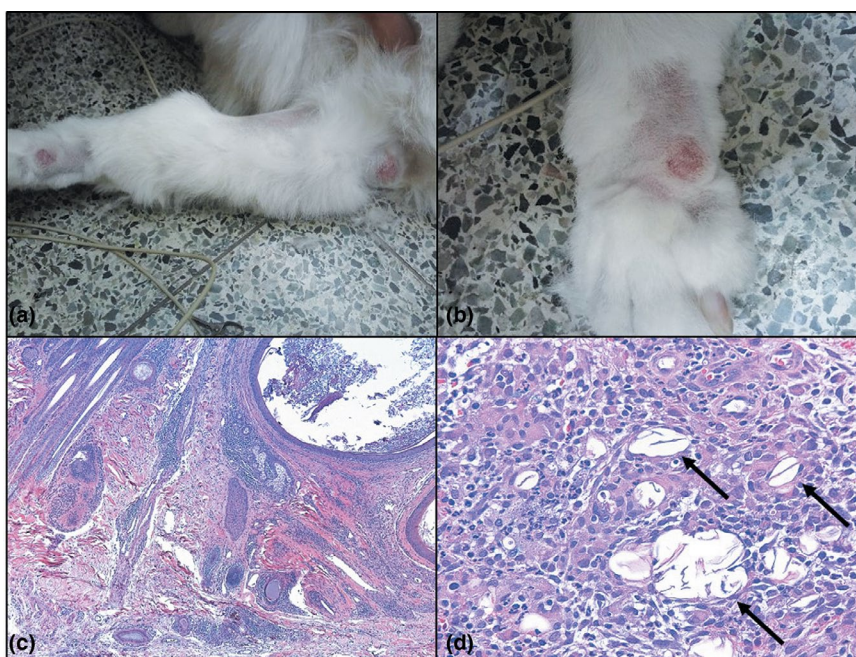


FIGURE 1 Multiple cutaneous nodules in a Samoyed dog (case 1). (a–b) Masses on the dorsal surface of the metacarpal bone and olecranon process of the left forelimb. (c–d) Histopathology of the cutaneous lesion in case 1. (c) Diffuse perifollicular inflammation and severely dilated follicle with keratins. H&E stain. $\times 10$. (d) The lesion predominantly consists of macrophages with several neutrophils and few giant cells and lymphocytes. Note the flaky keratins (arrows) surrounded by macrophages and giant cells. H&E stain. $\times 20$

bacterial contamination was detected in the ruptured crusted lesions; however, results of culture analyses of the intact masses were negative. Fine-needle aspiration cytology of the intact mass revealed numerous anuclear and keratinized squamous cells, possibly indicating matrical follicular cysts (Figure 3a). Moreover, the smear of the ruptured lesions showed a few keratinized squamous cells mixed with mucus, few metachromatic cells (suspected acinar cells), and numerous degenerating neutrophils (Figure 2a, b), indicating the spread of suppurative cellulitis into the salivary gland. The tentative diagnosis was aseptic suppurative cellulitis invading the salivary gland induced by foreign materials (e.g. keratin) from the cutaneous cyst.

Medical management for sialadenitis was initiated, including oral steroids (Prednisolone 0.5 mg/kg, PO, bid; LLOYD Inc., Shenandoah, USA) and Cyclosporine (5 mg/kg, PO, bid; Novartis, Basel, Switzerland).

Subsequently, surgical resection of the cysts was performed after resolution of inflammation around the tissue. Histopathologic examination of the resected masses revealed multiple infundibular cysts lined by squamous epithelium with a clear granular cell layer and central lamellar, flaky keratins (Figure 3b).

After 2 weeks, near-complete resolution of sialadenitis was observed, and the epidermal cysts were removed surgically (Figure 4a and b). The drugs were tapered over 2 months, and the disease was completely cured.

3 | DISCUSSION AND CONCLUSION

In the present study, we reported the occurrence of cutaneous pyogranulomas as foreign body reactions, initiated by keratins released

from ruptured follicular cysts irrespective of the type, infundibular or matrical. Although not life-threatening, this disease can deteriorate the quality of life in dogs.

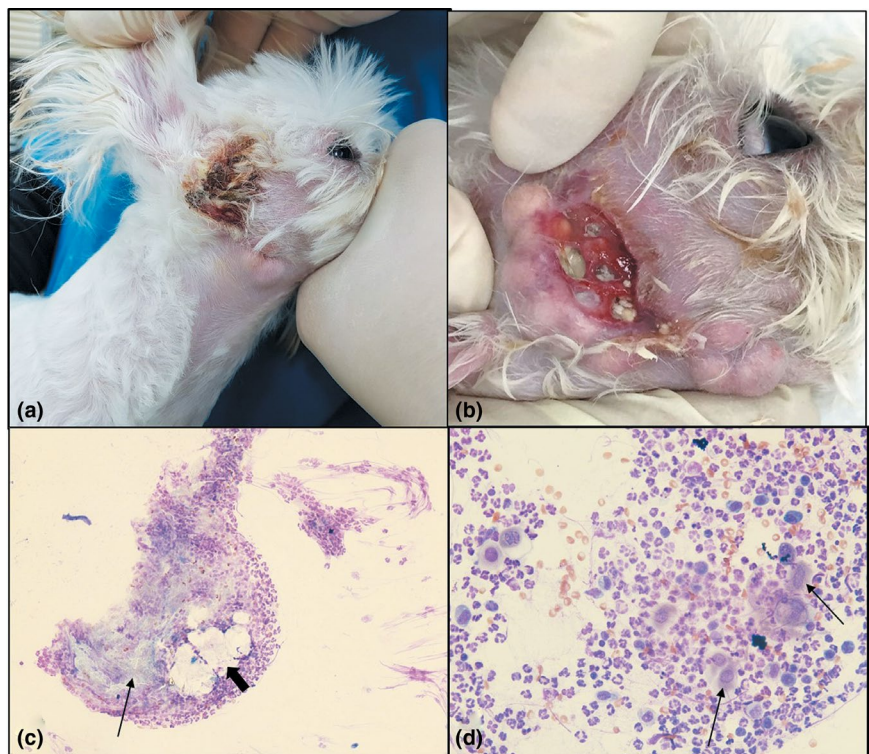
The central portion of follicular cysts contains keratin, not sebum, and often has a semi-solid appearance (Weir & St.Hilaire, 2019). Keratin is a water-insoluble protein, abundant in keratinocytes of the cornified layer in the epidermis (Lee et al., 2012; Weir & St.Hilaire, 2019). Keratin and hair shafts in the dermis trigger inflammatory reaction in the dermis and surrounding tissues following rupture of the cysts.

In humans, follicular cysts can be primary or secondary. Primary follicular cysts arise directly from the hair follicle through blockage of the lumen, whereas secondary epidermal cysts occur after implantation of the follicular epithelium in the dermis due to trauma or continuous mechanical pressure (Lee et al., 2013; Weir & St.Hilaire, 2019). Rupture of the cysts and extrusion of cystic contents into the surrounding cutaneous and subcutaneous tissues usually induce the inflammation.

Histopathology showed a pyogranuloma and moderate pyogranulomatous inflammation containing keratins in case 1. The dog showed signs of pain at the site of the lesions, which were located around pressure points, suggesting chronic irritation on the under-surface of the dog's body, resulting from living on a hard cement floor. Therefore, the dog's condition was possibly a case of secondary follicular cysts, consisting of pyogranuloma and pyogranulomatous inflammation induced by ruptured cyst. Surgery was not performed because the multiple lesions gradually resolved with only medication, and they were not easy to access with surgery.

Salivary gland disease may be elicited secondary response to trauma, systemic or localized infection, and immune-mediated

FIGURE 2 Pyogranulomatous sialadenitis and cutaneous cysts in case 2 (A Maltese dog). (a) Bloody and severely purulent crusted lesions around the salivary glands (parotid and submandibular). (b) After removing the crust, multiple holes are seen with ductal blockage presenting with whitish and semi-solid discharge. Multiple cutaneous cysts are present around the lesion. (c-d) Smear cytology of the discharge from the ruptured lesion. (c) Captured keratinized squamous cells (bold arrow) are surrounded by numerous degenerating neutrophils. Mucus with metachromatic cells (arrow) are also detected in the giant-cell complex. H&E stain. $\times 10$. (d) Another smear view of the discharge shows few macrophages with numerous degenerate neutrophils. The acinar cells of the salivary gland (arrows) are surrounded by pyogranulomatous inflammation. H&E stain. $\times 20$



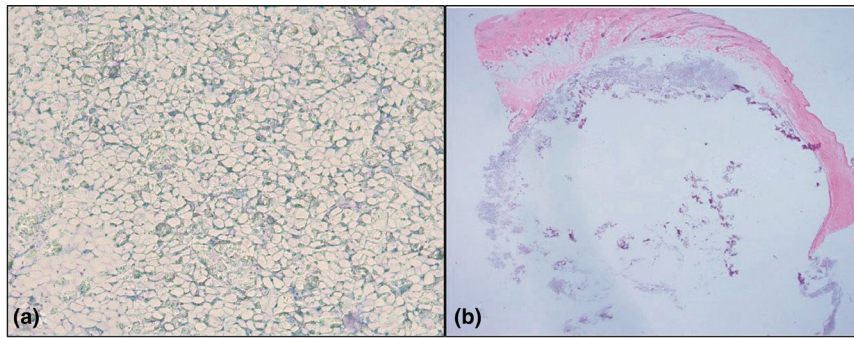


FIGURE 3 Cytology and histopathology of cutaneous cyst in case 2 after relieve inflammation. (a) Fine-needle aspiration cytology of the cutaneous cyst shows numerous anuclear keratinized cells. H&E stain. $\times 20$. (b) Histopathology of the cutaneous cyst shows severely dilated follicular cysts (matrical type) lined with basophilic, basaloid epithelium. H&E stain. $\times 10$



FIGURE 4 Progression of pyogranulomatous sialadenitis and cutaneous cysts in case 2 (a Maltese dog). (a) After 2 weeks of medical treatment, the ruptured inflammatory lesion has almost disappeared; however, multiple cutaneous cysts persisted. (b) Two months after surgical removal, the lesions resolved completely

disease in dogs (Harvey, 1989; Spangler & Culbertson, 1991). Case 2 was associated with sterile sialadenitis caused by ruptured gland ducts that were connected with epidermal cysts in the dermis. The dog also showed signs of pain at the site of the lesions, which were ulcerated and inflamed. The material in the cysts invaded the salivary glands through the ducts, and the ducts were obstructed by the foreign contents of the cysts. Obstruction and invasion caused by the material from the epidermal cysts may have induced sialadenitis.

The biopsy was conducted after resolution of inflammation in the surrounding tissues because ruptured secondary lesions can affect the results of histopathological analysis. Therefore, there was no direct evidence of foreign body material invasion to the salivary glands from the ruptured ducts on histopathology. We could analyse the pathogenesis based on only cytological analysis and clinical outcomes. Further studies relating mechanism are needed to clarify.

The present cases were successfully managed with anti-inflammatory and immunosuppressive drugs: steroids and cyclosporine. The foreign body response begins with rapid neutrophil accumulation and the fast adsorption of various host proteins to foreign material in acute stage (Lee & Kim, 2015). In chronic phase,

the role of macrophage interaction with inflammatory cytokines (e.g. tumour necrosis factor- α , Interleukin-1 β , Interleukin-6) is dominant (Chu et al., 2020) The immune suppressive drugs might work well relating those mechanisms.

Based on the clinical outcomes, immune-mediated aetiology caused by foreign bodies was strongly suspected. However, no surgical procedures were attempted owing to the presence of multiple granulomas that were located in the extremities and at flexible points in case 1. Fortunately, the granulomas disappeared without surgery. In other words, case 2 was successfully managed with immunosuppressive pharmacological therapy and surgery.

The present case reports highlight the manifestation of canine epidermal cysts at specific sites due to trauma or obstruction. Foreign body reactions due to rupture of epidermal cysts or ducts are associated with immune-mediated inflammation surrounding the tissue. Surgical excision and immunosuppressive pharmacological therapy may be required for management of the condition.

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CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

AUTHORS CONTRIBUTION

Ha-Jung Kim: Conceptualization; Investigation; Visualization; Writing-original draft. **Kyoung-Oh Cho:** Investigation; Visualization; Writing-review & editing. **Yeong-Bin Baek:** Investigation; Visualization; Writing-review & editing.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The dogs' owners gave permission for the publication of this clinical case.

PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1002/vms3.542>.

DATA AVAILABILITY STATEMENT

All data supporting our findings are included in this study.

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