pISSN 1598-298X / eISSN 2384-0749
J Vet Clin 36(6) : 345-348 (2019)
http://dx.doi.org/10.17555/jvc.2019.12.36.6.345

Journal of Veterinary Clinics
www.ksvc.or.kr

Cutaneous Sterile Pyogranuloma/Granuloma Syndrome in an Old English Bulldog: Case Report

Ji-Seon Yoon, Hyeona Bae*, Soomin Ahn*, Il-Hwa Hong*, Dong-In Jung*, Jinho Park and DoHyeon Yu*[1]

College of Veterinary Medicine, Chonbuk National University, Iksan 54596, Korea
**College of Veterinary Medicine, Gyeongsang National University, Jinju 52828, Korea*

(Received: November 07, 2019 / Accepted: November 28, 2019)

Abstract : A four-year old, indoor-living neutered male Old English Bulldog was presented for generalized ulcerative dermatitis. Generalized alopecia and multifocal papules and ulcers with crusting were observed mainly in the dorsal trunk. Cytology of the skin lesions revealed a pyogranulomatous inflammation comprising macrophages and nondegenerate neutrophils. Histopathology also revealed a nodular dermatitis characterized by mixed infiltration of monocytes and neutrophils involving the superficial and deep dermis. Neither of bacteria nor fungus was identified in microscopic exam and culture. From those findings, a diagnosis of cutaneous sterile pyogranuloma/granuloma syndrome (SPGS) was made. Treatment with immunosuppressive drugs of prednisone and cyclosporine was performed and visible ulcerative skin lesions were resolved after 4 weeks of initiation of therapy. Treatment with combination of cyclosporine and prednisone may be effective for the case of SPGS.

Key words : sterile pyogranuloma/granuloma syndrome, idiopathic dermatitis, dog.

Introduction

Cutaneous sterile pyogranuloma/granuloma syndrome (SPGS) is idiopathic, uncommon canine skin disorder (6). The definition of sterile is based on the exclusion of other possible etiological agents such as microorganisms and foreign body (2). The etiology and pathogenesis of cutaneous SPGS is currently unknown, although a good response to systemic glucocorticoids suggests the involvement of immune-mediated mechanisms (9). Skin lesions can be observed in any skin lesion, although usually observed on the bridge of the nose, muzzle, periocular region, pinnae, and paws (6,7). The primary lesions of SPGS represent papules and nodules, which are multiple, well demarcated, solid, elevated, and sometimes greater than 1 cm in diameter. However, they are easily ruptured and ulcerated (3). Diagnosis of SPGS is based on clinical appearance, histopathological findings and lack of microorganisms and foreign bodies (2).

Herein, we describe the successful treatment of canine cutaneous SPGS which presented with generalized ulcerative dermatitis. Cutaneous SPGS was diagnosed by histopathologic findings and negative results for bacterial and fungal culture.

Case Presentation

A four-year old, indoor-living neutered male Old English Bulldog was presented for generalized ulcerative dermatitis. The lesions have progressed to crusting and multifocal ulcers over a period of 1 month. Prior to being referred, antibiotic was administered for 4 weeks for superficial pyoderma from a local veterinary clinic, but it was not responsive.

On physical examination, the dog presented with multifocal non-pruritic ulcerative skin lesions, which comprised generalized alopecia and multifocal papules with crusting. The skin lesions were mainly observed in the dorsal trunk, extending from the neck to the front of the tail (Fig 1A and B). Body temperature was elevated up to 40.0°C. General dermatological examinations, bacterial and fungal culture, skin biopsy, and histopathological examinations as well as blood works were performed at the time of referral.

The results of hematologic analysis and survey radiographs were not significant. Impression smears after punch biopsy were obtained from the ulcerative skin lesions and stained by the Diff-Quik. Cytology revealed non-degenerative neutrophils, macrophages and spindle shaped cells originated from metaplasia secondary to inflammation (Fig 2A and B). Meanwhile, acantholytic keratinocytes, bacteria and *Malassezia* spp. were not observed. Parasitic infestation such as demodicosis was ruled out by skin scraping examination.

The skin lesions were then subjected to bacterial and fungal culture, and punch biopsy. Specimens were collected using a 4 mm punch biopsy from skin lesions on the dorsal trunk. The biopsies were fixed on cardboard in 10% buffered formalin for histopathological analysis. Sections were processed for histopathological evaluation, and stained with hematoxylin and eosin (H&E). Histopathology revealed a nodular dermatitis characterized by cellular infiltrate in perifollicular areas oriented in the dermis and subcutis (Fig 3A). The predominant inflammatory cells were macrophages and neutrophils (Fig 3B). Other findings such as necrosis, microorganisms and foreign bodies were not observed. In addition, bacterial

[1]Corresponding author.
E-mail : yudh@gnu.ac.kr

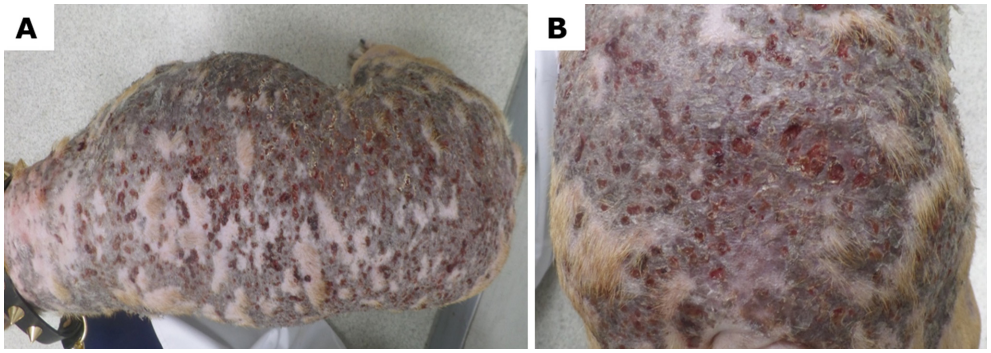

Fig 1. Clinical findings of the present case at the initial presentation. On physical examination, multifocal ulcerative skin lesions were observed in the dorsal trunk extending from the neck to the front of the tail (A). The ulcerative skin lesions comprised alopecia and multifocal papules with crusting (B).

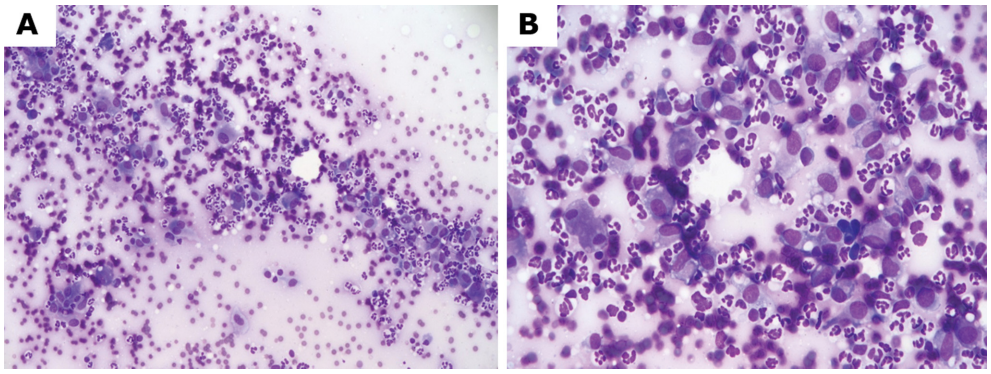

Fig 2. Cytology of the impression smear. Cytology revealed many non-degenerative neutrophils, macrophages and spindle shaped cells originated from metaplasia secondary to inflammation (A) × 400 (B) × 1000.

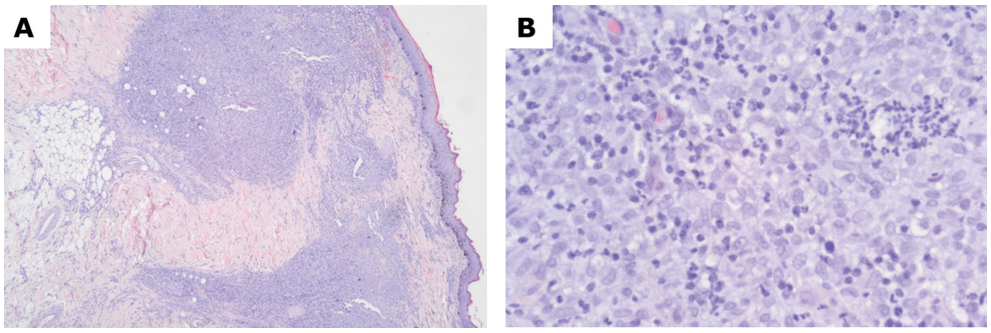

Fig 3. Histopathological findings of the present case. Nodular and diffuse infiltration of large numbers of inflammatory cells were observed in superficial and deep dermis (A) Infiltrated cells were mainly macrophages and neutrophils (B). Other findings such as necrosis, microorganisms and foreign bodies were not observed (Hematoxylin and eosin staining).

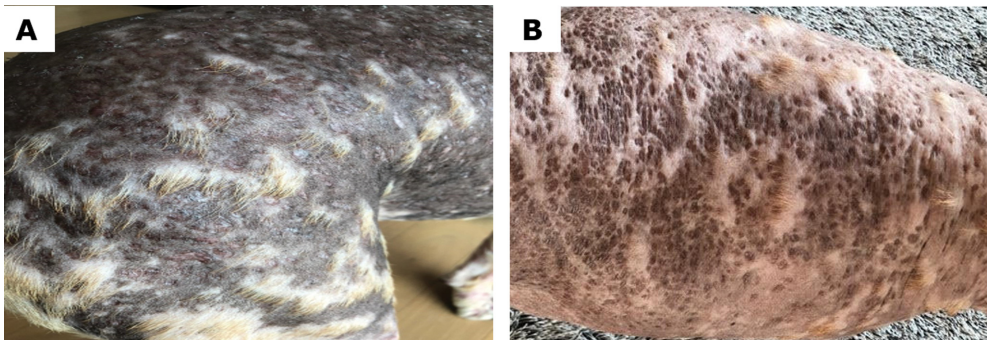

Fig 4. Resolution of clinical sings after treatment of immunosuppressive drugs. After 4 weeks of treatment, the ulcerative skin lesions were no longer visible (A). No recurrence was observed until 5 months of initial treatment, although hair regrowth was not observed (B).

and fungal culture revealed negative for infectious agents. Based on the findings, the present dog was diagnosed with SPGS and treatment with immunosuppressive drugs of prednisone (2 mg/kg, SID) and cyclosporine (5 mg/kg, SID) was performed. One week after the initiation of therapy, the ulcerative dermatitis improved and visible ulcerative skin lesions were resolved after 4 weeks of initiation of therapy (Fig 4A). Treatment with cyclosporine was then discontinued and the dosage of prednisone was successfully tapered to a low dose. In addition, no recurrence was observed until 5 months of initial treatment, although hair regrowth was not observed (Fig 4B).

Discussion

SPGS usually represents with plaque, nodules and ruptured nodules with draining tracts (2). However, the present case showed extensive multifocal ulcerative dermatitis in overall trunks from neck to tails. From the clinical signs, skin diseases which induce ulcerative dermatitis such as cutaneous lymphoma, erythema multiforme, cutaneous vasculitis, and toxic epidermal necrolysis rather than SPGS were included in the top of differential diagnosis. However cytology and histopathological findings corresponded with the characteristics of SPGS. Therefore, this case report demonstrates that the clinical signs of SPGS can be seen as extensive multifocal ulcerative dermatitis, and thus the possibility of SPGS should be considered when multifocal ulcerative dermatitis is seen in dogs. In addition, multifocal ulcerative dermatitis was considered as moderate to severe SPGS and treatments with two immunomodulators of cyclosporin and prednisone were effective for the case of moderate to severe SPGS.

The diagnosis of cutaneous SPGS is challenging and can be made by histopathologic findings and ruling out other granulomatous and pyogranulomatous skin diseases (2). Cytology of skin lesions in the present case revealed non-degenerative neutrophils and macrophages and histopathologic findings also revealed a nodular dermatitis characterized by mixed infiltration of monocytes and neutrophils which were mostly involved in the superficial and deep dermis. Therefore, the present case was thought to have granulomatous and pyogranulomatous skin diseases. The granulomatous and pyogranulomatous skin diseases can be caused by either infectious agents or noninfectious agents (8). Infectious agents are associated with protozoans, mycobacteria, pathologic dimorphic fungi. Noninfectious agents are mostly associated with foreign body (8). A diagnosis of cutaneous SPGS can be made after ruling out infectious agents and non-infectious agents (3). In the present case, neither causative organisms nor foreign bodies were detected by histopathology, impression smears and culture. From those findings, a diagnosis of SPSG was made in the present case.

Treatment of SPGS includes immunomodulation. The choice of immunomodulator is usually associated with the degree of clinical severity (9). For moderate to severe presentations, the use of prednisolone concurrent with secondary immunomodulator is suggested. Cyclosporine is known as reliable steroid-sparing control for moderate to severe cases of SPGS (9). The present case showed multifocal ulcerative skin lesions in overall dorsal trunk and thus the patient was considered as moderate to severe SPGS. Therefore, immunosuppressive therapy was initiated using combination of prednisone and cyclosporine and the ulcerative lesions were resolved after 4 weeks of treatment. Secondary use of cyclosporine in addition to prednisone may be effective for the case of moderate to severe SPGS.

Although ulcerative skin lesions were resolved, hair regrowth was not observed until 5 months of treatment. Similar findings of non-regrowth of hair were observed in a previous case of multiple SPGS (3). This might be due to significant inflammation involving the dermis and subcutis where the hair follicles are located. In particular, the bulge region which are located in isthmus part of hair follicles, contain stem cells that are crucial for hair and skin regeneration (4,5). The significant inflammation involving the dermis and subcutis might induces the destructions of hair follicle bulge region and thus hair regrowth was not observed in the present case even though visible ulcerative skin lesions were resolved after treatments.

A previous study reported that the microorganisms of mycobacteria and *Leishmania* were detected using a polymerase chain reaction (PCR) technique in specimens although previously diagnosed as SPGS (1,8). Therefore, ruling out of the cause of granulomatous and pyogranulomatous skin diseases needs to involve a multidisciplinary diagnostic approach including PCR to detect mycobacteria and *Leishmania*. One of the potential limitations of our study was that PCR technique to rule out mycobacteria and *Leishmania* was not conducted in the present case. Nonetheless, a good response for immunomodulation therapy indicates the low possibility of the presence of mycobacteria and *Leishmania* in the present case. The use of the PCR technique should be considered to rule out the presence of *Leishmania* or mycobacteria in pyogranulomatous/granulomatous skin lesions.

Cutaneous SPGS is an idiopathic, uncommon canine skin disorder. This case report describes a case of canine SPGS which shows multifocal ulcerative dermatitis in overall trunk. Treatments with combination of cyclosporine and prednisone may be effective for the case of moderate to severe SPGS.

Acknowledgment

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (NRF-2017R1D1A1B03034904).

References

1. Cornegliani L, Fondevila D, Vercelli A, Mantero G, Fondati A. PCR technique detection of Leishmania spp. but not Mycobacterium spp. in canine cutaneous 'sterile' pyogranuloma/granuloma syndrome. Vet Dermatol 2005; 16: 233-238.
2. Gross TL, Ihrke PJ, Walder EJ, Affolter VK. Noninfectious nodular and diffuse granulomatous and pyogranulomatous diseases of the dermis. In: Skin diseases of dog and cat: Clinical and histopathologic diagnosis. 2nd ed. Oxford; Blackwell Publishing. 2005; 320-323.
3. Kawarai S, Matsuura S, Yamamoto S, Kiuchi A, Kanemaki N,

Madarame H, Shirota K. A case of cutaneous sterile pyogranuloma/granuloma syndrome in a maltese. J Am Anim Hosp Assoc 2014; 50: 278-283.
4. Kobayashi T, Iwasaki T, Amagai M, Ohyama M. Canine follicle stem cell candidates reside in the bulge and share characteristic features with human bulge cells. J Invest Dermatol 2010; 130: 1988-1995.
5. Mercati F, Pascucci L, Gargiulo AM, Dall'Aglio C, Ceccarelli P. Immunohistochemical evaluation of intermediate filament nestin in dog hair follicles. Histol Histopathol 2008; 23: 1035-1041.
6. Panich R, Scott DW, Miller WH. Canine cutaneous sterile pyogranuloma/granuloma syndrome: A retrospective analysis of 29 cases (1976-1988). J Am Anim Hosp Assoc 1991; 272: 519-528.
7. Santoro D, Spaterna A, Mechelli L, Ciaramella P. Cutaneous sterile pyogranuloma/granuloma syndrome in a dog. Can Vet J 2008; 49:1204-1207.
8. Santoro D, Prisco M, Ciaramella P. Cutaneous sterile granulomas/pyogranulomas, leishmaniasis and mycobacterial infections. J Small Anim Pract 2008; 49: 552-561.
9. Schissler J. Sterile Pyogranulomatous Dermatitis and Panniculitis. Vet Clin North Am Small Anim Pract 2019; 49: 27-36.