Opis przypadku *Case report*

Case of cutaneous sterile pyogranuloma/granuloma syndrome in a Standard Schnauzer

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Summary

Canine cutaneous sterile pyogranuloma/granuloma syndrome (SPGS) is an uncommon skin disease in dogs and cats. Clinical manifestations are skin lesions such as papules, nodules and plaques; however, nodules are the most commonly described lesions in the course of cutaneous sterile pyogranuloma/granuloma syndrome. These lesions can be single or multiple, diffuse or limited to a small area. The affected area can become alopecic. In some cases ulcerations and secondary bacterial infections may occur. The characteristic nodules are firm, well demarcated from the surrounding tissue and no pruritic with varying size between a few millimeters to a few centimeters. Histiocytic nature of the inflammatory infiltrate, the absence of the pathogen and a good response to glucocorticoid therapy suggest an autoimmune nature of the disease; however, etiology and pathogenesis remain unknown for sure. When response to steroid therapy is unsatisfactory, niacinamide, tetracycline and azathioprine are used or surgical removals of the lesions are applied. In the reported case, skin lesions were successfully treated for 6 months with prednisolone. Cutaneous sterile pyogranuloma/granuloma syndrome was diagnosed by excluding other disorders and by histopathology which revealed dermatitis with inflammatory infiltrate that was characterized by moderate histiocytic and neutrophilic along with sparse lymphocytes and plasma cells. Moreover no pathogen was found in PAS staining.

Keywords: pyogranuloma, cutaneous, sterile, canine

Cutaneous sterile pyogranuloma/granuloma syndrome is an uncommon skin disease in dogs. No age or gender predisposition is reported so far. However, this condition seems to be observed more often in Boxers, Collies, Great Danes, Weimaraners and Golden Retrievers. The clinical manifestations are papules, nodules and plaques. The lesions can be single or multiple, diffuse or limited to a small area and can become alopecic. The characteristic nodules are firm, well demarcated from the surrounding tissue and non-pruritic. Their size varies between a few millimeters to a few centimeters. In some cases ulcerations and secondary bacterial infections may occur (2, 5, 6). Lesions are usually observed on the head, paws and less often on pinnae and abdomen region. Systemic signs such as lymphadenopathy and hypercalcemia are rare. Histopathological manifestations are nodular or diffuse lesions infiltrating the superficial dermis (2, 3). Etiology and pathogenesis remain unknown; however, the histiocytic nature of the inflammatory infiltrate, the absence of pathogens and a good response to glucocorticoid therapy suggest an autoimmune nature of the disease (1, 2, 4). The diagnosis is based on clinical symptoms, the result of a histopathology and ruling out the presence of pathogens (2, 5, 6). In some cases, *Leishmania* spp. infections and leproid granuloma syndrome (CLGS) can imitate histopathological and clinical picture of cutaneous sterile pyogranuloma/granuloma syndrome (4). Therefore it is essential to exclude the possibility of travel into the endangered areas.

Case report

A 6-year-old, female Standard Schnauzer weighing 21 kg was presented with multiple nodules on the head and non-specific disease symptoms such as weakness and apathy. The clinical examination revealed several firm, well demarcated nodules of varying diameter (few millimeters to 1.5 cm) associated with alopecia affecting the head. The area where the nodules appeared was alopecic (Fig. 1A). The hair on the ventral aspect of the thorax, abdomen and tail was thinned. The lesions started as papules 4 weeks earlier and had increased progressively in number and size over time.

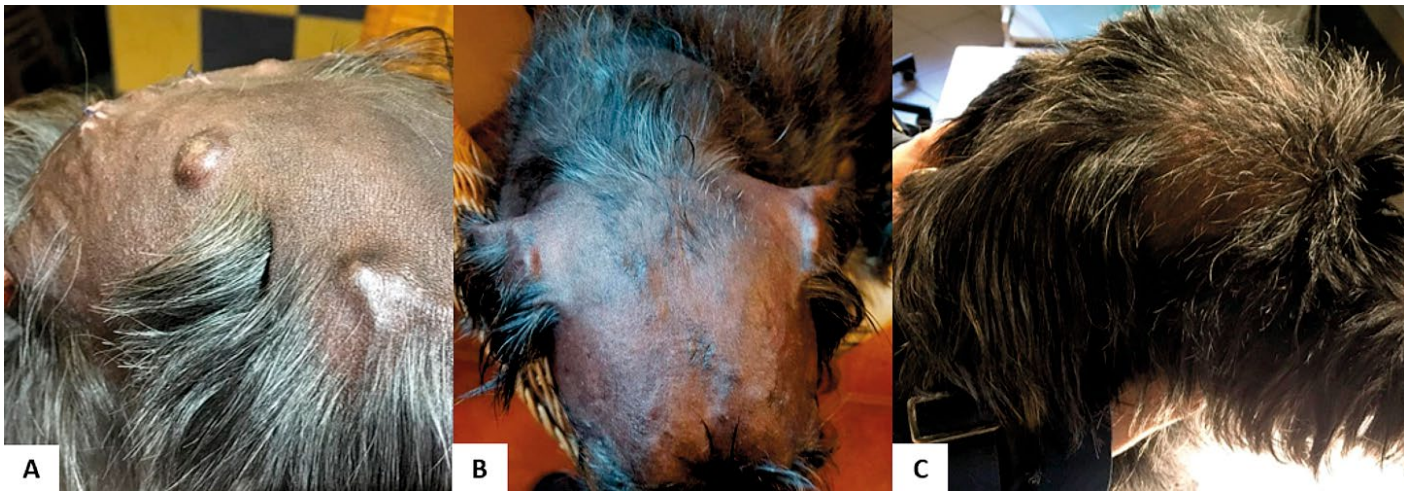

Fig. 1. Pictures showing a patient with Canine sterile pyogranuloma/granuloma syndrome. (A) Patient before treatment. Photographs showing nodules on the head and alopecia. (B) Patient undergoing treatment with glucocorticosteroids. Visible improvement of the condition of the skin on the head and hair growing back. (C) Patient after 6 months of therapy

Tab. 1. Total blood count before treatment, serum biochemical panel, ionograms and the concentration of the thyroid hormones

Analyte	Value	Reference range
WBC	9.9 × 10^9/L	6.0-17.0
RBC	9.48 × 10^9/L	5.5-8.5
HGB	18.2 × 10^9/L	11.0-19.0
HCT	54.6%	39.0-56.0%
MCV	72.0 fL	62.0-72.0
MCH	22.2 pg	20.0-25.0
MCHC	35 g/dL	30.0-38.0
RDW	11.9%	11.0-15.5
PLT	389 × 10^9/L	117-460
MPV	8.9 fL	7.0-12.9
PDW	16.4	
PCT	0.364%	
ALT	35.4 U/l	3.0-50.0
ASP	36.44 U/l	1.0-37.0
ALP	95.17 U/l	20.0-155.0
Amylase	965.9 U/l	388.0-1800.0
BUN	25.61 mmol/l	0.0-50.0
CR	0.9 µmol/l	0.6-1.8
Glucose	95 mmol/l	60-120
Potassium	4.88 mmol/l	4.1-5.4
Na	150.9 mmol/l	139.1-156.5
Chloride	99.1 mmol/l	96-113
Ca, total	2.98 mmol/l	2.1-3.0
Phosphorus	5.06 mg/dl	2.5-6.3
Magnesium	2.53 mg/dl	1.7-2.9
Iron	101.8 µ/dl	80-178
T4	3.18 µg/dl	1.5-4.5
fT4	1.463 ng/dl	0.6-3.7
Cholesterol	6.09 mmol/l	3.1-8.6

The temperature was 38.4°C, mucous membrane of the oral cavity were pink and moist with capilar refill time less than 2 seconds. No cardiac nor pathological respiratory murmurs were found. A regular heart rate was 100 beats per minute. Also no pathologies were found in the electrocardiographic, echocardiographic or abdomen ultrasound examination. RTG revealed Th4-Th7 discospondylosis. A complete blood count, a serum biochemical panel, ionograms (Śląskie Laboratoria Analityczne Vet) and the concentration of thyroid hormones were performed (VetLab Katowice) (Tab. 1).

Multiple deep skin scrapings were obtained from lesions at the head and were negative for the presence of *Demodex canis*. Mycological culture for yeast-derived fungi and dermatophytes was negative as well. Cushing's syndrome was ruled out by performing a dexamethasone suppression test at low-dose (IDEXX) (Tab. 2).

Cytological examination by fine-needle aspiration (with 23 gauge needle and 5 milliliter syringe) from plaques at the head. Six smears were developed and did not give an unequivocal result due to the solid nature of the nodules, therefore a skin punch biopsy (Fig. 2A) was performed. The biopsies were obtained from plaques on the head using sedation with 0.6 mg, IM, of medetomidine (Cepetor; Scanvet, Gniezno, Poland) and butorphanol 0.4 mg, IM (Butomidor; Orion-Pharma, Warsaw, Poland) and were fixed in 10% buffered formalin for histopathological analysis. Sections were processed for histopathological evaluation and stained with hematoxylin and eosin (H&E). Sections were also stained with periodic acid-Schiff (PAS) but no pathogens were found (IDEXX). The histopathological examination showed nodular to diffuse dermatitis infiltrated by numerous neutrophils, epithelioid macrophages and rare lymphocytes and plasma cells (Fig. 2B). The polymerase chain reaction (PCR) technique for the presence of *Leishmania* spp. and

Tab. 2. Result of dexamethasone suppression test at low-dose

Analyte	Value (Reference range)
Cortisol value before dexamethason supply	99.8 nmol/l (24.8-124.2)
4 hour after cortisol supply	4.9 nmol/l
8 hour after cortisol supply	3.1 nmol/l

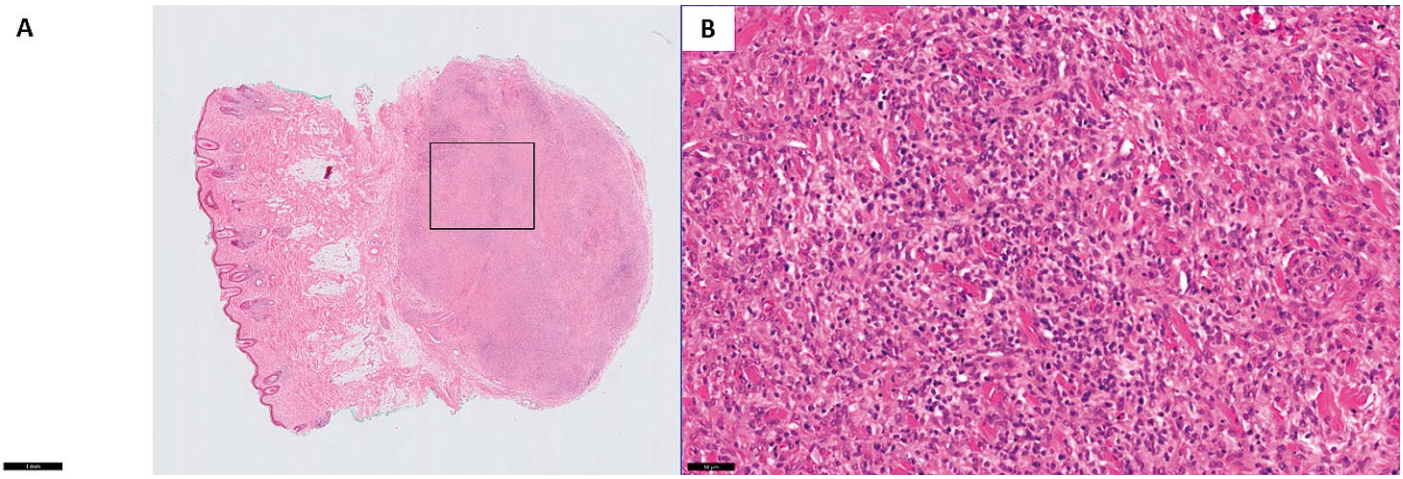

Fig. 2. Photomicrographs showing obtained punch biopsy. (A) Photomicrograph of the nodule obtained by punch biopsy. (Hematoxilin & eosin; Bar = 1 mm); (B) Photomicrograph depicted on the inflammatory infiltrate characterized by a predominance of numerous neutrophils, epithelioid macrophages, lymphocytes, plasma cells and small amounts of loose collagenous tissue. (Hematoxilin & eosin; Bar = 50 µm)

Mycobacterium spp. was not performed due to the low probability of these pathogens in Poland.

This histopathological picture revealed cutaneous sterile pyogranuloma/granuloma syndrome. Treatment with immunosuppressive dose of prednisolone 2.5 mg/kg body weigh p.o. q 24 hr had been administrated. After five days the nodules became smaller; however, due to the deterioration of the dog's condition (vomiting and apathy) it was decided to reduce the dose of prednisolone, initially to 1 mg/kg body weight and then to 0.5 mg/kg body weight p.o. q 24 hr. Despite the dose reduction, further improvement was observed. New hair appeared in the previously alopecic areas (Fig. 1B). After 6 months therapy hair regrowth almost completely and all of the skin lesions disappeared (Fig. 1C).

Discussion

There are hypotheses that cutaneous sterile pyogranuloma/granuloma syndrome may be a response to pathogens such as *Leishmania* spp. and *Mycobacterium* spp., although some authors underline only the similarity of the symptoms. However it is essential to rule out the presence of these pathogens (5). Treatment is based on surgical removals of the lesions and/or pharmacological therapy using immunosuppressive doses of glucocorticoids (2.5 mg/kg body weight p.o. q 24 hr of prednisolone). Lower dose of prednisolone (0.4-1.1 mg/kg body weight p.o. q 48 hr) is used to prevent a relapse (1). Since pharmacological treatment is effective in most cases it should be initially applied and only if the result is unsatisfactory, surgical removal should be considered. Niacinamide, tetracycline and azathioprine are used if the response to steroid therapy is poor (2). Azathioprine is an antimetabolite and shows strong immunosuppressive effect. It is used in a dosage of 1 mg/kg body weight p.o. q 24 hr in combination with prednisolone. It is mandatory to use antibiotics in case of secondary bacterial infections. The combination of tetracycline and niacinamide has an immunomodulatory effect. Niacinamide blocks mast cell degranulation and inhibits release of leukocyte protease, while tetracycline is able to inhibit complement cascade, antibody production, leukocyte chemotaxis, prostaglandin synthesis and the production of lipases and collagenases. Their combination has the ability to inhibit leukocyte blast transformation as well as the neutrophils and eosinophils chemotaxis (2, 5). In dogs weighing less than 10 kg, a dose of 250 mg of tetracycline and niacinamide per animal is used, and in dogs weighing more than 10 kg 500 mg of both drugs per animal is used p.o. q 8 hr (2). To summarize, the pathogensis is still unknown but good response to glucocorticoids, immunomodulating drugs and histiocytic nature of the inflammatory infiltrate suggests an autoimmunological nature of this disorder (5).

A cutaneous sterile pyogranuloma/granuloma syndrome is a diagnostic challenge for the veterinarian. This disease is similar with other skin lesions which appear due to bacterial and parasitological infections. Even some neoplastic skin lesions can have similarities with cutaneous sterile pyogranuloma/granuloma syndrome. Therefore a multidisciplinary approach is necessity.

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