An atypical case of pyoderma gangrenosum in a dog

Een atypisch geval van pyoderma gangrenosum bij een hond

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ABSTRACT

Neutrophilic and ulcerative dermatitis is reported in a mixed breed dog. The condition was considered to be an atypical case of pyoderma gangrenosum. Clinically, it had a more superficial ulceration, a more pronounced pustular component and lacked the characteristic cutaneous pain and tenderness of the lesions. The diagnosis of pyoderma gangrenosum was made as a diagnosis of exclusion. The dog showed an excellent response to treatment with ciclosporin (Cyclavance, Virbac, Leuven, Belgium).

SAMENVATTING

In deze casuïstiek wordt een geval van neutrofiele en ulceratieve dermatitis beschreven bij een canis vulgaris. De aandoening werd beschouwd als een atypisch geval van pyoderma gangrenosum. De hond had een uitgesproken pustulaire eruptie en vertoonde meer oppervlakkige ulceraties. Ook ontbrak bij deze letsels de voor pyoderma gangrenosum karakteristieke begeleidende pijn. De diagnose van pyoderma gangrenosum werd gesteld als een diagnose per uitsluitsel. De hond vertoonde een uitste-kende respons op een behandeling met ciclosporine (Cyclavance, Virbac, Leuven, Belgium).

INTRODUCTION

Pyoderma gangrenosum (PG) is a rare, chronic, often destructive, inflammatory skin disease, in which a nodule or pustule breaks down to form a progressively enlarging ulcer with a raised, tender, and undermined border. Lesions may be solitary or multiple and are, almost invariably painful (Gross et al., 2005; Ruocco et al., 2009). They present either in the absence of any apparent underlying disorder or in association with a systemic disease, or may more rarely be linked to many kinds of surgery and various drugs (Ruocco et al., 2009). PG is largely a clinical diagnosis based on clinical features and exclusion of all other causes of ulcerative skin disease (Gross et al., 2005; Ruocco et al., 2009). The histopathology of PG is unspecific and shows massive dermal infiltrations of neutrophils and large crateriform ulcers with neutrophils beneath and adjacent to the ulcers (Gross et al., 2005; Ruocco et al., 2009). The primary objective of biopsy is to rule out other causes of ulceration, i.e. infection, vasculitis, malignancy.

Four clinical and histological variants of PG have been described in humans, i.e. ulcerative, pustular, bullous and vegetative (Weedon, 2002; Ruocco et al.,2009). There is still little information available regarding the characteristics of PG in dogs as only a few cases have been reported in the peer-reviewed literature (Bardagi et al., 2007; Simpson et al., 2013; Declercq, 2015; Nagata et al., 2016). Affected dogs may be febrile and have malaise (Gross et al., 2005). Reported canine PG cases are all typical forms with cutaneous lesions described as painful and deep ulcerative. PG in the dog has a predilection for the trunk, particularly the dorsum (Gross et al., 2005), although limbs, head and neck, tail base and tail, may also be involved (Declercq, 2015). The phenomenon of pathergy or Koebner phenomenon, i.e. new lesions forming in response to minor trauma (Simpson et al.,2013; Nagata et al., 2016) and the clinical finding of cribriform scarring (Simpson et al., 2013), minor human diagnostic criteria, have been documented. Reported effective treatments in the dog include oral prednisolone alone (Declercq, 2015; Nagata et al., 2016) or in conjunction with ciclosporin (Bardagi et al., 2007) or with azathioprine (Simpson et al.,2013).

The aim of this report was to describe an atypical case of PG in a dog.

Figure 1. Large and deep draining ulceration on the head. Note the ectropion of the right lower eyelid.

Figure 2. Distribution of the lesions. Note the large and deep ulceration on the head in contrast to the more superficial aspect of the small ulcers on the body and limbs.

CASE DESCRIPTION

A seven-year-old, mixed breed, spayed, female dog was presented to the referring veterinarian with a fever of 40°C and skin lesions. Pustules and crusts were observed on the bridge of the nose, the dorsal trunk and on the limbs. The lesions were not pruritic or painful. One month prior to the onset of the skin condition, the dog had a dental care treatment for periodontal disease and ten days prior to the onset of the skin condition, the dog underwent surgery for a closed-cervix pyometra. At both of the medical interventions, the dog had been treated with eight-day courses of oral amoxicillin clavulanate (Clavubactin, Le Vet B.V., Oudewater, the Netherlands) 15 mg/kg twice daily and five-day courses of meloxicam oral suspension (Meloxoral, Le Vet B.V., Oudewater, the Netherlands) 0.1 mg/kg once daily. An adverse drug reaction was suspected and all drugs were stopped. Skin biopsies were obtained and submitted for histopathology. The morphologic diagnosis was neutrophilic vasculitis. Treatment with prednisolone (Prednisolone, Kela Laboratories, Sint-Niklaas, Belgium) 2 mg/kg once daily was initiated. Clinical response to immunosuppressive doses of prednisolone was excellent. Dose tapering to 1 mg/kg by the referring veterinarian resulted in severe worsening of the skin problem. The dose of prednisolone was increased to 1.5 mg/kg and ciclosporin (Cyclavance, Virbac, Leuven, Belgium) 6 mg/kg once daily was added. As the dog was febrile and new pustular lesions still had developed over the following few days, the case was referred. In order to fully evaluate the original nature of the dog's skin lesions, the referring veterinarian was advised to stop all immunosuppressive medications. Within the next three days, a deep and exudative ulceration reappeared on the dog's face. Therefore, in the meantime to the referral, a treatment was dispensed of oral enrofloxacin (Baytril, Bayer, Diegem, Belgium) 5 mg/kg once daily combined with oral clindamycin (Clindamycine, Kela Laboratories, Sint-Niklaas, Belgium) 10 mg/kg twice daily.

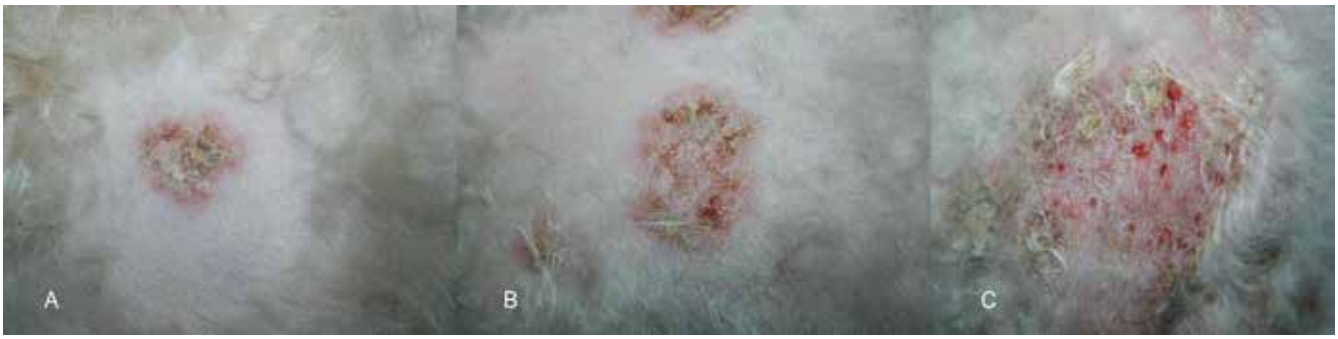

Figure 3. PG lesions on the trunk in various stages of development. A. Well-demarcated clusters of small yellow pustules on an erythematous base. B. The pustules are breaking down to form small ulcers and new pustules are arising at the border. C. Small superficial indolent ulcers with no undermined borders that do not drain.

At admission, the dog was depressed and had a normal rectal temperature. Physical examination revealed widespread skin disease. There were lesions on the face, the medial aspect of both ears, on the dorsolateral neck and trunk, and on the four limbs. The initial lesions were small pustules that broke down to form ulcers. The skin disease was non-painful, neither at the pustular stage nor at the ulcerative stage. The face was more severely affected. There was widespread and deep ulceration with exudation and crusting that had deformed the lower right eyelid causing ectropion (Figure 1). Lesions on other parts of the body, i.e. medial aspects of the ears, neck and trunk, limbs were characterized by multifocal, well-demarcated areas that were studded with small pustules, arising simultaneously or subsequently, on an erythematous base. Pustules broke down to form small and indolent superficial ulcers that did not drain. Peripheral spreading of these focal areas resulted from new pustules arising on the erythematous periphery. The lesions on the legs had coalesced to involve almost the entire limbs (Figures 2 and 3). The peripheral lymph nodes were normal on palpation. Differential diagnosis included, but was not limited to, deep bacterial pyoderma, fungal infection and pyoderma gangrenosum.

Cytology and bacterial culture of intact pustules, and fungal culture and skin biopsies of truncal lesions were performed. Cytological evaluation of the pustule's contents revealed numerous neutrophils and a few macrophages suggesting a purulent-pyogranulomatous inflammation. No microorganisms were detected in any of the cytology samples. While awaiting the findings of both of the cultures and the results of the histopathological examination, the combined antibiotic therapy was continued. At twenty days of treatment, there was no improvement of the skin lesions. Histopathological examination revealed focal and dense subepidermal, neutrophilic infiltrations, not primarily follicular, with dermal hemorraghes (Figure 4). There were multiple crateriform ulcers covered with neutrophils that occasionally penetrated into the deep dermis (Figure 5). No microorganisms were identified on histopathology, on hematoxylin and periodic acid-Schiff stains. No bacterial or fungal growth was obtained from the submitted skin samples.

Pyoderma gangrenosum was diagnosed by exclusion diagnosis. Antibiotics were stopped. Treatment with oral ciclosporin 6.5 mg/kg once daily was initiated. Ten weeks later, the skin lesions had progressively resolved and the treatment was continued, given once every second day for one month and then given once every third day for two months. Therapy was stopped, but seven weeks later, new pustular lesions developed. Treatment with once-daily oral ciclosporin was reinstituted for a month and the dog was finally maintained in remission with six days of treatment a week. There was cicatricial alopecia and permanent scarring of the face (Figure 6).

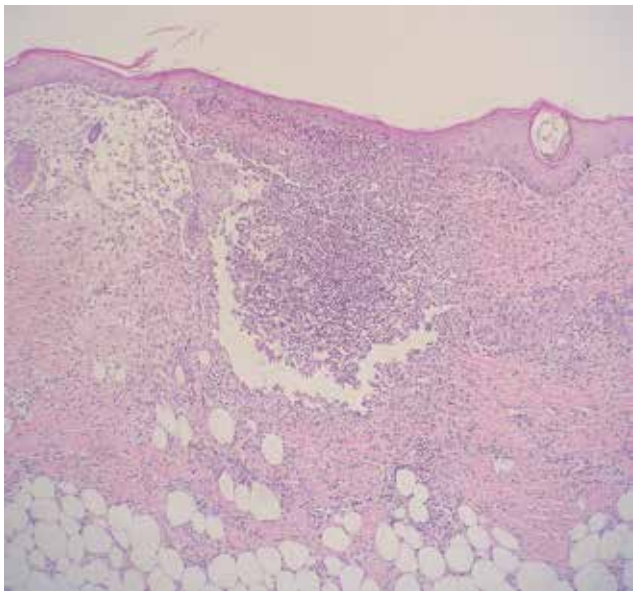

Figure 4. Subepidermal neutrophilic infiltration, not primarily follicular. Note the subepidermal hemorraghe (hematoxylin and eosin stain 200x).

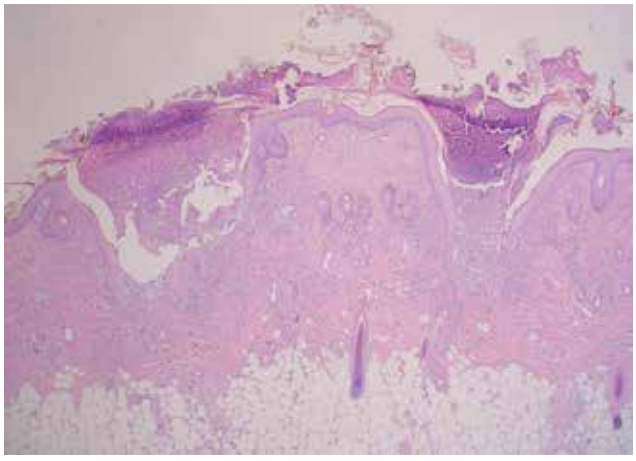

Figure 5. Early ruptured dermal pustules. Small crateriform superficial ulcers with grossly no undermined peripheral borders (hematoxylin and eosin stain 40x).

Figure 6. Healing of the lesions after ciclosporin therapy. Note the cicatricial alopecia and the scarring of the face.

DISCUSSION

PG is a rare inflammatory and ulcerative skin disease of presumed neutrophilic dysfunction (Gross et al., 2005; Ruocco et al., 2009). As histopathology is indicative, but not diagnostic, the diagnosis rests entirely on the clinical presentation and course. Typical clinical features include a painful pustule or nodule that breaks down to form a progressively enlarging deep ulcer with a raised, tender, undermined border that drains exudate. Peripheral growth results from the burrowing extension of the undermined margin or from fresh pustules arising on the border. Lesions may be solitary or multiple, gradually progressive or indolent (Gross et al., 2005; Ruocco et al., 2009). In humans, clinical variants have been described where the ulceration is more superficial and with no undermined border or surrounding erythema (Weedon, 2002; Ruocco et al., 2009). In doubtful atypical cases, the diagnosis is confirmed through a process of elimination of other (infectious) causes of cutaneous ulcers (Ruocco et al., 2009).

The primary skin lesion in the dog of the present report was a small pustule that broke down to form an ulcer. Peripheral growth resulted from new pustules arising on the border. On the dog's head, the lesions had progressed and coalesced to form a deep and large ulceration. On all other parts of the body, pustules had appeared in well-demarcated clusters with a surrounding erythema. The resulting ulcers remained small and superficial and did not drain. There was no pain at any stage of the disease and the peripheral lymph nodes were normal. Except for malaise, there were no systemic signs. The skin condition in the present report was considered to be an atypical case of PG for several reasons. First, the dog presented with an overlap of different types of PG. It had the classical deep ulceration of PG on the head that was progressive and draining. In other parts of the body, there was a more superficial ulceration and a pronounced pustular component. The small ulcers were indolent and had no undermined borders. Secondly, severe pain and tenderness commonly associated with lesions of PG, were not present at any stage of the disease. Lesions in humans have been reported as, almost invariably, painful (Ruocco et al., 2009). This wording may imply that cutaneous pain is not an absolute criterion for diagnosis and it may occasionally be absent. The lesions involved the head, dorsolateral neck and trunk, and limbs, which fits with the description in published canine PG cases.

In atypical cases, as in the present case, the diagnosis is based on exclusion of other causes of similar appearing cutaneous ulcerations. Fungal infection was excluded by a negative culture on Sabouraud's dextrose agar and a negative periodic acid-Schiff staining of the skin biopsies. Cytology samples and bacterial culture of intact pustules could not detect the presence of bacterial microorganisms. The lack of response to antibiotics of different classes, i.e. beta-lactams, fluoroquinolones, lincomycin, and the excellent response to prednisolone and ciclosporin supported a non-infectious etiology of the dog's skin condition. The histopathology findings observed in this dog were similar to those seen in PG, i.e. massive neutrophilic dermal infiltrations (subepidermal pustulations) and crateriform ulcers. Histopathological examination of the skin biopsies, initially obtained by the referring veterinarian, had provided a morphologic diagnosis of neutrophilic vasculitis. This misdiagnosis could be related to the choice of the biopsy site that lacked the massive dermal neutrophilic infiltration. Histopathology of PG may show pronounced dermal hemorrhages (Gross et al., 2005) and a vasculitis may be present as a secondary event (Weedon, 2002). Taken into consideration the pathology result, exclusion of other causes and failure to respond to anti-infectious agents, the diagnosis of PG was made as a diagnosis of exclusion.

Underlying conditions could not be identified. PG has been rarely linked with various drugs and surgery (Gross et al., 2005; Ruocco et al., 2009; Miller et al., 2013). Interestingly, prior to the onset of the skin lesions, the dog of the present report and a dog in another report had been treated with meloxicam (Declercq, 2015). The dog of the present case had developed PG soon after abdominal surgery. Triggering of PG by the administered meloxicam or by surgery cannot be completely discarded.

The number of cases of PG in the veterinary literature is too small to draw any meaningful conclusions regarding comparative treatments. The dog in the present report had been treated consecutively with prednisolone alone, prednisolone in conjunction with ciclosporin and ciclosporin alone. The therapeutic responses to these treatments suggested that concurrent short-term use of prednisolone at an immunosuppressive dose with ciclosporin may be considered as an effective treatment of PG in dogs.

In summary, PG can be a challenging clinical diagnosis. Dogs may present with atypical lesions characterized by a more florid pustular component and a more superficial ulceration that lacks an undermined border, which is normally seen. Cutaneous pain is not an absolute clinical criterion for the diagnosis and it may be absent.

REFERENCES

Bardagi M., Lloret A., Fondati A., Ferrer L. (2007). Neutrophilic dermatosis resembling pyoderma gangrenosum in a dog with polyarthritis. *Journal of Small Animal Practice 48*, 229-232.

Declercq J. (2015). A case of pyoderma gangrenosum in a dog successfully treated with prednisolone alone. *Vlaams Diergeneeskundig Tijdschrift 84*, 158-161.

Gross T.L., Ihrke P.J., Walder E.J., Affolter V.K. (2005). Canine pyoderma gangrenosum. In: Gross T.L., Ihrke

P.J., Walder E.J., Affolter V.K. (editors). *Skin Diseases of the Dog and Cat: Clinical and Histopathologic Diagnosis*. Second edition, Blackwell Publishing, Oxford, p.132-134.
Miller W.H., Griffin C.E., Campbell K.L. (2013). Pyoderma gangrenosum. In: Miller W.H., Griffin C.E., Campbell K.L. (editors). *Muller and Kirk's Small Animal Dermatology*. Seventh edition, Elsevier Mosby, Missouri, USA, p.709-710.
Nagata N., Yuki M., Asahina R. et al. (2016). Pyoderma gangrenosum after trauma in a dog. *The Journal of Veterinary Medical Science 78*, 1333-1337.
Ruocco E., Sangiuliano S., Gravina A.G., Miranda A., Nicoletti G. (2009). Pyoderma gangrenosum: an updated review. *Journal of the European Academy of Dermatology and Venereology 23*, 1008-1017.
Simpson D.L., Burton G.G., Hambrook L.E. (2013). Canine pyoderma gangrenosum: a case series of two dogs. *Veterinary Dermatology 24*, 552-555.
Weedon D. (2002). Pyoderma gangrenosum. In: Weedon D. (editor). *Skin Pathology*. Second edition, Elsevier Science Limited, London, p.251-252.

Uit het verleden

'T ZWIEN

Het zwien is het schoonste der beesten,
Zonder varken wuk zouden we zyn?
't Is er nodig ip al onze feesten,
Ik eet'n alles gèren van 't zwien.

Smout, vet, hespe en spek, hoofdvlees, korteletten en paté
Worsten en bloeling en vette derms, scheutelvlees en zwienepoot.

E'j gie nog dat beestje zien slokken?
't Is altijd zo up zyn gemak.
Het jeunt hem in sop en in brokken,
Zijn pootjes staan ook in de bak.

In 't zwienekot, ge zoudt daar wegsleeren,
Niet dat de zwiens daarmee afzien.
Ze wroeten, ze zoen 't ol ommekeren,
Hoe vulder, hoe schoonder om zien.

Een plaatje die ook nog kan tellen
Voor 's winters os 't vriest gereed te doen:
Een schoon stuksje zwienerauwélle,
Met kole gestoofd in andjoen.

Die gerenoars, 'k kan geen meer rieken,
En koeietong, 'k wil geen meer zien.
En zwijg me van haze of kieken,
Mo geef mi een broksje van 't zwien.

Liedje gebracht door de folkgroep O'Djavel. Auteur van de tekst: F. Vercruysse