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Pemphigus Foliaceus in a Labrador retriever: A case report

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Abstract
Pemphigus foliaceus is the most common autoimmune skin disease in dogs and cats. The clinical signs are macules, pustules, erosions, erythema, crusts, and hyperkeratosis; usually on the nasal planum, eye margin, ear pinna, and foot pad; or generalized lesions with alopecia and pruritus. A two-year-old female Labrador was presented to the small animal medicine unit of the veterinary clinical complex, VCRI, Namakkal with erythematous lesions present on the nasal planum and around both the eyes for three days before presentation. Acantholytic cells were observed in cytology, confirming the condition as pemphigus foliaceus. Oral immunosuppressive drugs and antibiotics were advised for two weeks. The animal made complete remission and no recurrence has been observed thus far.

Keywords: Autoimmune skin disease, crust, cytology, immunosuppressive drugs

Introduction
Pemphigus complex is a group of autoimmune skin diseases, characterized by acantholytic pustules followed by crusting, encountered in dogs and cats. Autoantibodies against desmosomal proteins lead to loss of cell-to-cell adhesion of keratinocytes, causing loss of integrity of the epidermal cell layers. This results in transient pustules that later form erosions, crusts, scales, and alopecia on the skin and/or mucous membranes. Five forms of pemphigus have been identified based on the distribution of lesions and desmosomal protein targeted: pemphigus foliaceus (PF), pemphigus erythematosus (PE), pan-epidermal pustular pemphigus, pemphigus vulgaris, and paraneoplastic pemphigus (Rosenkrantz, 2004) [7]. In a nutshell, PF and PE cause superficial lesions and the target protein is desmocollin I (DSC-I); while PV causes deep ulcerated lesions at the mucocutaneous junction, the targeted protein being desmoglein-3 (DSG-3), (Almela and Chan, 2021) [6]. Pemphigus foliaceus is the form most frequently recorded in pet animal practices. It may occur spontaneously or may be associated with drugs, environmental factors, or concurrent autoimmune diseases.

Case history and clinical observation
A two-year-old female Labrador was presented with a history of erythematous swelling around the eyes and on the nasal planum, which developed gradually over three days, accompanied by intense pruritus. The lesions were erythematous, pustular, and crusty. Erosion and bleeding caused by self-mutilation were also seen. No other generalized skin lesions of significance were evident. On physical examination, congested mucous membrane, elevated rectal temperature (104.5°F) and lymphadenopathy were recorded while other vital parameters were within the normal range. Skin scrapings were negative for mites. Touch impression was taken by rupturing intact pustules and stained with Diff-Quik stain. Numerous neutrophils and clusters of acantholytic keratinocytes were visualized, which were indicative of either chronic skin infection or pemphigus. Based on the acute onset and superficial distribution of the lesions with unaffected mucocutaneous junctions, the condition was tentatively diagnosed as pemphigus foliaceus.

Treatment
Due to the severe but localized nature of the lesions treatment with topical immunosuppressive ointment and supportive oral medications for 14 days were opted. Tacrolimus ointment (Ichmune T ®) was applied twice daily at 12 hours intervals. Tablets of doxycycline (10 mg/kg, s.i.d, after food) and pantoprazole (1mg/kg, s.i.d, before food) were advised along with

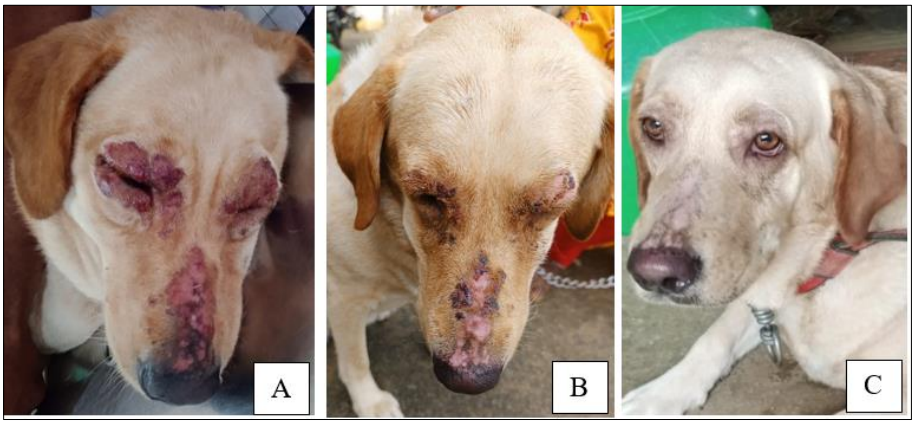
niacinamide supplement, syrup Pregamyl Boost ® (500mg niacinamide b.i.d). E-collar was advised through the course of treatment to prevent excoriation due to itching and scratching. Three days post-start of treatment, there was a mild reduction in erythema, swelling, and pruritus. By day ten, the lesions had reduced gradually with no pruritus. On day twenty remission of lesions with signs of hair regrowth was observed. The animal made a complete recovery, within two weeks and no recurrence has been reported thus far.

Table 1: Hematological evaluation showed leukocytosis and neutrophilia

Parameters	Normal range	Observed value
Haemoglobin (g/dl)	12 - 19	15.6
PCV (%)	37 - 57	50
RBC (* 10^6 / cumm)	5.0 – 9.0	7.18
WBC (* 10^3 /cumm)	5.0 – 15.0	16.16
Neutrophil (%)	60 - 75	78
Lymphocyte (%)	18 - 21	17.1
Monocyte (%)	2 - 10	4.9
Platelets (10^5 / cumm)	1.6 - 5.1	4.8

Table 2: All serum biochemical values were within the normal ranges

Parameters	Normal range	Observed value
Total Protein (g/dl)	5.4 – 7.1	6.57
Albumin (g/dl)	2.3 – 3.3	3.0
ALT (U/L)	10 – 109	52.8
BUN (mg/dl)	8 – 28	10
Creatinine (mg/dl)	0.5 – 1.8	1.1
Calcium (mg/dl)	9.0 – 11.7	10.2
Phosphorus (mg/dl)	2.6 – 5.3	5.83
Glucose (mg/dl)	65 - 118	67



a) Day of presentation: Erythematous swelling with papules and erosions.
b) Day 10: Reduced swelling and dried crust with evident healing
c) Day 20: Complete healing with hair regrowth

Fig 1: Gradual response to treatment

Discussion

Pemphigus foliaceus is the most common autoimmune skin disease in dogs and cats. This condition is defined by the production of autoantibodies against Desmocolin I (DSC I), a subunit of adhesion molecules on keratinocytes (Merilraj *et al.* 2022) [3]. The most frequent cause of pemphigus foliaceus is idiopathic, which is also associated with ultraviolet rays, certain medications (such as sulphonamide, cephalexin, amoxicillin-clavulanic acid, etc.), and potential long-term effects of chronic inflammatory skin disease (Olivry T, 2006) [5]. Akita and Chow Chow breeds are genetically predisposed, according to Mueller et al. (2006) [4], although Labradors and Dobermans are more susceptible to drug-induced pemphigus foliaceus. The owner in this case reported that the animal was kept indoors and hadn't recently taken any medications, thereby pointing to an idiopathic etiology. According to Takayama and Busch (1991) [2], different animals develop lesions at different rates. There are two types of lesions: localized (limited to the nasal planum, periorbital region, ear pinna, and foot pads) and generalized (bilateral symmetric lesions with severe pruritus). The current case was severe, localized, and accompanied by severe pruritus. Similar to this case, the lesions start out pustular or blister-like throughout several hair follicles before rupturing and forming thick, yellow crusts. In chronic conditions, erosions and cracks are seen along with severe discomfort and limbing. Systemic symptoms may also include fever, anorexia, limb edema, and lymphadenopathy, which was present in this case (Mueller *et al.* 2006) [4]. According to Almela and Chan (2021) [6], alterations in total blood counts can include mild to moderate neutrophilia, moderate to notable leukocytosis, and mild non regenerative anemia. Biochemical tests may also reveal minor hypoalbuminemia and modest globulin elevations. Diagnosis of pemphigus foliaceus is through cytology, histopathology, and immunofluorescence test. Pemphigus foliaceus has a number of alternative diagnoses, all of which were ruled out

in this instance, including superficial pyoderma, pustular dermatophytosis, demodicosis, lupus erythematosus, pododermatitis, and hypothyroidism.

According to Rosenkrantz, (2004) [7] treatment options can be adopted depending on the severity of lesions. Tacrolimus or hydrocortisone ointment applied twice a day along with oral adjunctive therapy- Niacinamide and Doxycycline, with/without Cyclosporine, is ideal for mild and localized conditions. For moderately severe conditions oral immunosuppressive drugs like prednisolone, dexamethasone, triamcinolone, or oclacitinib (Apoquel) are preferred individually or in combination (Olivry *et al.* 2006) [5]. Tapering the dose of steroids to avoid adverse effects and appropriate maintenance dose for remission, should be taken care of. In the present case systemic immunosuppressive drugs were avoided due to localized lesions and remission was noticed by topical application of tacrolimus ointment, twice a day, along with doxycycline and niacinamide supplementation. In a study by Edginton *et al* (2011) [1] used a combination of Tetracycline and niacinamide to treat dogs with superficial pemphigus in 34 dogs and observed promising results in comparision to treatment with immunosuppressive drugs alone. Tetracyclines like doxycycline bind to calcium and prevent complement activation, antibody production, and chemotaxis. Niacinamide, too prevents leucocyte chemotaxis, as well as inhibits synthesis of pro-inflammatory cytokines and maintains epidermal skin barrier.

Conclusion

Pemphigus should be considered in cases with lesions on the nasal planum and periorbital regions, along with foot pads. The presence of acantholytic cells in cytology is suggestive of Pemphigus foliaceus, while immunofluorescence provides confirmation. Onset, distribution of lesions, clinical signs, presence of acantholytic cells in cytology in the absence of dermatophytes and response to treatment can be considered for diagnosis of Pemphigus foliaceus. It is ideal to treat superficial mild pemphigus foliaceous with topical immunosuppressive ointment along with tetracycline and niacinamide combination orally. Prompt diagnosis of the condition is essential for early and complete remission of the condition.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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