Case Report

CLINICAL MANAGEMENT OF PEMPHIGUS USING AZATHIOPRINE IN A LABRADOR RETRIEVER

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ABSTRACT

An array of autoimmune diseases that cause blisters and damage to the skin and mucous membranes is known as the pemphigus complex. It is marked by the development of autoantibodies directed towards keratinocyte adhesion molecules. Clinical signs include crusts, erosions, erythema, macules, pustules and hyperkeratosis. These lesions are typically found on the foot pad, nasal planum, ear margins and ear pinna etc. There can also be generalized lesions accompanied by pruritus and alopecia. A five-year-old female Labrador was brought with erythematous lesions around nose, periorbital area, ears, foot pads and vulva for three days prior to presentation. Cytology revealed acantholytic cells, indicating that the problem was pemphigus. For six weeks, oral immunosuppressive azathioprine and other supportive medications like ranitidine, fexofinadine and niacinamide were recommended. The animal experienced total recovery following treatment.

Keywords: Azathioprine, dog, pemphigus

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A set of autoimmune disorders known as the pemphigus complex impact the skin and mucous membranes, resulting in the development of shallow or deep blisters (Tavakolpour, 2017). For a variety of frequently unclear reasons, the immune system begins to manufacture antibodies directed against specific desmosome segments - the multiprotein complexes that hold neighbouring keratinocytes together. These auto-antibodies are known as pemphigus antibodies. The various subtypes of antibodies target distinct desmosome antigens that are expressed in various layers of the epidermis (Ferreira *et al*., 2019). Based on the pattern of lesions and the desmosomal protein targeted, five types of pemphigus have been recognised: pemphigus vulgaris, pemphigus erythematosus, pan-epidermal pustular pemphigus, pemphigus foliaceus, and paraneoplastic pemphigus (Molla *et*

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al., 2016). In summary, desmocollin-I is the target protein for pemphigus foliaceus and pemphigus erythematosus caused lesions, whereas desmoglein-III is the target protein for pemphigus vulgaris caused lesions. The type that is most commonly observed in pet animal practices is Pemphigus foliaceus. It could happen on its own or be brought on by medications, the environment, or coexisting autoimmune conditions.

An intact female Labrador, age five, was brought to the medicine section of Referral Veterinary Polyclinic at ICAR-IVRI, Izatnagar with a history of pruritus and moist erythematous lesions (bilaterally symmetrical) surrounding eyes, nasal planum, concave aspect of ear pinnae, around anus and vulva(Fig. 1). The lesions occurred over a period of three days. The lesions initially started at ears and then spread to eyes, nostrils, paws and vulva. There were also signs of self-mutilation due to pruritus. There were no more noticeable widespread skin lesions. Bathing was done once in 15 days and no history of external parasites was reported.

During the physical inspection, the patient had a congested mucous membrane and a slightly raised rectal temperature (103.5°F), but all other vital signs were within normal limits. Tests on skin scrapings revealed no mites. An additional skin scraping was cultured on SDA (Sabouraud Dextrose Agar) and yielded negative results. Lactophenol cotton blue for fungus investigation revealed no evidence of fungal infection. A touch impression was obtained, which was then stained with Giemsa stain. A collection of acantholytic keratinocytes (Fig. 2) and a large number of neutrophils were observed; these cells suggested that the patient had either pemphigus or a long-term skin infection. The illness was tentatively identified as pemphigus due to the disease's abrupt onset, distribution of lesions and ruling out other possibilities.

Treatment with oral immunosuppressive along with supplementary medications was chosen due to the acute but localised nature of the lesions. Tablets of azathioprine (Imuran®) @ 2 mg/kg body weight q24h orally for 15 days were given and then tapered gradually over one month. The supportive therapy included ranitidine (Rantac®) @ 2 mg/kg body weight q12h orally for 10 days, fexofenadine (Allegra®) @ 5 mg/kg body weight q12h orally for 3 days, Pregamyl Boost ® syrup @ 500 mg of niacinamide q12h orally. Throughout the course of treatment, wearing an e-collar was advised to prevent mutilation from itching.

One of the most prevalent cutaneous autoimmune diseases in dogs, Pemphigus complex is linked to the generation of detrimental autoantibodies that primarily attack epidermal adhesion proteins (Merilraj *et al*., 2022). Breakdown of intercellular adhesion molecules results in lesions in pemphigus. When this interaction damages tissue, inflammatory cells and acantholytic keratinocytes are produced, which are seen in cytological analyses. It can be troublesome to treat canine pemphigus therapeutically, and immunosuppressive drugs are frequently needed. Medications that

negatively modulates immune activation, like azathioprine and prednisolone, are used to manage this inflammatory response. The foundation for treating Pemphigus is steroid medication. However due to its side effects, systemic therapy with corticosteroid-sparing medications is advised (Porro *et al.*, 2019). Azathioprine is one of them and it works by preventing humoral and cellular immune responses. In order to prevent adverse reactions to the medication, a gradual tapering off of steroid therapy was initiated following improvements in clinical condition. Niacinamide hinders the production of pro-inflammatory cytokines (such as IL-1β, IL-6, IL-8, TNF), stops leucocyte chemotaxis, and preserves the epidermal skin barrier. When described lesions are present on the foot pads, periorbital areas, and nasal planum, pemphigus should be considered. Although immunofluorescence confirms the diagnosis, the presence of acantholytic cells in cytology is indicative of Pemphigus. Pemphigus can be diagnosed based on a number of factors, including the lesions' distribution, onset, clinical signs, presence of acantholytic cells in the cytology sample when dermatophytes are absent, and response to treatment. The lesions progressively decreased and were no longer itchy by day 15. The lesions were cleared up by day 40, along with indications of hair regrowth. Six weeks later, the animal recovered fully (Fig. 3), and there have been no reports of a recurrence since.

Fig.1. Moist erythematous lesions (bilaterally symmetrical) surrounding eyes, nasal planum, concave aspect of ear (A, B, C), around anus and vulva (D).

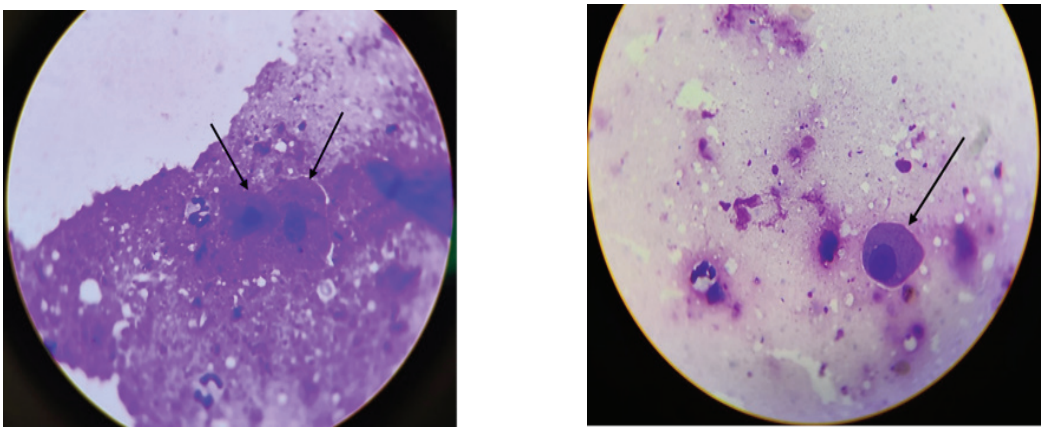

Fig.2. Acantholytic cells were found - round, ovoid or "fried egg" shaped, with a deeply basophilic, centrally located nucleus. Acantholysis occurs due to loss of cohesion between epidermal cells due to the breakdown of intercellular bridges.

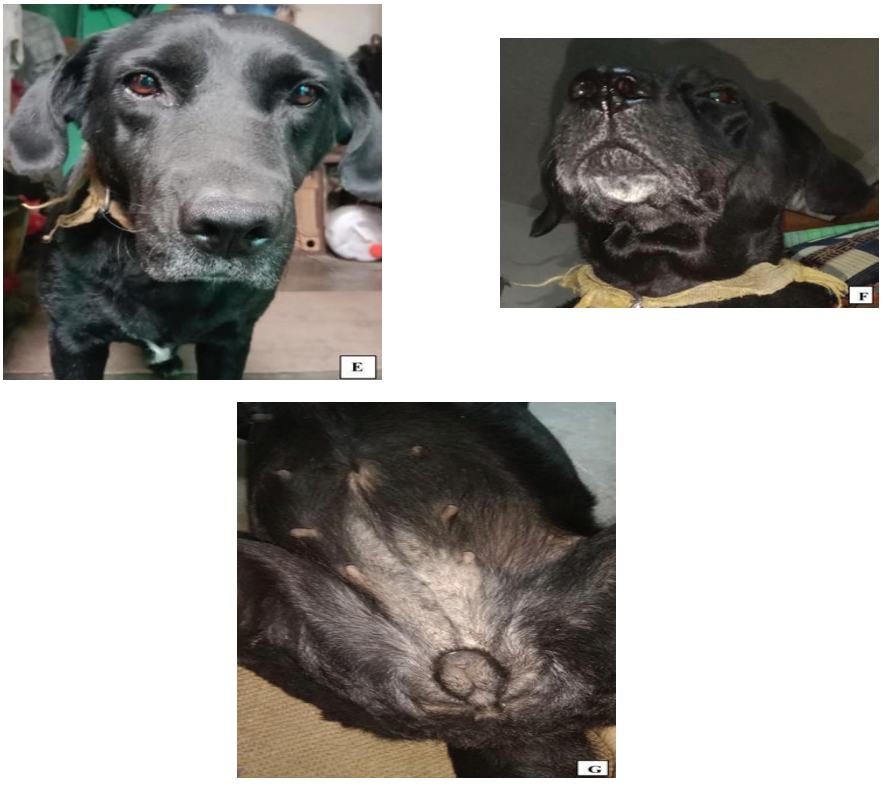

Fig.3. Labrador dog showing improvement in condition three months after treatment with azathioprine and supportive therapy (E,F,G).

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