

# “Pemphigus Foliaceus in the Canine”

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## **INTRODUCTION**

Pemphigus foliaceus is the most common dermatologic autoimmune disease in dogs.<sup>2,4,6</sup> Pemphigus foliaceus is a superficial type of pemphigus in a complex of pemphigus diseases.<sup>11</sup> There are two variants of this complex such as superficial pemphigus, pemphigus foliaceus and pemphigus erythematosus, and deep types like paraneoplastic pemphigus and pemphigus vulgaris.<sup>4,11</sup> In pemphigus foliaceus autoimmune antibodies attack the integrity of the skin by breaking down the bridges that hold the epidermal cells together.<sup>6,8</sup> Clinical signs such as lesion localization can help determine the type pemphigus a dog has and the severity of the disease. There are multiple factors in what causes pemphigus foliaceus. There are also some breeds that are more affected than others.

This paper will focus on pemphigus foliaceus and its disease process. Clinical signs, breed predispositions, and diagnostics will be covered as well. The treatment modalities, such as immunosuppressive therapy, and prognosis of this disease will also be discussed.

## **HISTORY AND PRESENTATION**

Pemphigus foliaceus is an autoimmune disease that is commonly seen in middle aged dogs, but dogs of any age and gender can be affected.<sup>6,8</sup> The breeds that are more predisposed to acquiring pemphigus foliaceus are: Akitas, Chow Chows, Doberman Pinschers, Dachshunds, and Newfoundlands.<sup>3,6,7</sup> The primary lesion of pemphigus foliaceus is a pustule. These lesions typically begin along the nasal bridge, around the eyes, and the pinnae of the ears.<sup>2,6</sup> It is typical for the lesions to spread and occur along the trunk, feet, clawbeds, groin, and footpads.<sup>2,6</sup> In most cases, the pustules form and rupture very quickly and are rarely seen.<sup>2,6</sup> Instead, we often observe areas of hair loss, yellow-brown dried crusts, redness and scale.<sup>2,6,8</sup> These skin lesions are variably pruritic.<sup>2,6</sup> Severely affected animals may become anorexic, depressed and have a

fever.<sup>6</sup> Some dogs may develop a secondary bacterial infection due to breach in integument. The disease itself often displays a waxing/waning course.<sup>6</sup>

## **PATHOPHYSIOLOGY**

Pemphigus foliaceus is a dermatologic autoimmune disease that affects the integrity of the integument by disrupting the cell to cell matrix.<sup>4</sup> Epidermal cells, or keratinocytes, are adhered together by structures known as desmosomes. In the disease process of pemphigus foliaceus autoimmune antibodies attack structural proteins within the desmosomes known as desmocollin-1.<sup>7</sup> In humans the major autoantigen for pemphigus foliaceus is desmoglein-1, and recent studies have shown that desmoglein-1 is a minor autoantigen in canine pemphigus foliaceus.<sup>7</sup> When the desmocollin-1 is disrupted, the cells become separated from each other and the epidermis loses its intercellular connections.<sup>7</sup> The breakdown of this component causes the outer layer of skin to split apart and blister.<sup>6</sup> This process is called acantholysis, when the deposition of antibody in intercellular spaces causes the cells to detach from each other within the uppermost epidermal layers.<sup>8</sup> Pustule formation occurs when neutrophils infiltrate the area.<sup>10</sup> Pemphigus foliaceus can develop spontaneously, without a discernible cause.<sup>6</sup> There are several triggering factors that can lead to pemphigus foliaceus. Topical products containing amitraz, contained in a previous product called Promeris, used for demodectic mange and flea and tick control, is considered a trigger.<sup>3</sup> Another suspected trigger is chronic skin allergies.<sup>4,8</sup> Certain prescription drugs that have been linked to cause a reaction and lead to pemphigus foliaceus are penicillin, cephalosporins, and sulfonamides.<sup>4,8</sup> Environmental factors such as exposure to sunlight and ultra-violet rays have been considered a trigger for pemphigus foliaceus as well.<sup>4,8</sup>

## **DIAGNOSTIC APPROACH /CONSIDERATIONS**

Pemphigus foliaceus can be diagnosed tentatively through clinical signs and cytology of a pustule.<sup>2,4</sup> To obtain a definitive diagnosis, a skin biopsy ideally containing an intact pustule should be submitted for histopathology.<sup>2,4</sup> A suggestive diagnosis from cytology should reveal numerous acantholytic keratinocytes collected from a pustule.<sup>4</sup> These acantholytic keratinocytes can be free floating or in clusters.<sup>4</sup> These cells can also be seen in a mix of nondegenerate neutrophils and rare eosinophils.<sup>4</sup> Acantholytic keratinocytes exhibit either microscopic characteristics of normal differentiated spinous or granular layer epithelial cells, or they present signs of apoptosis with eosinophilic cytoplasm, condensed chromatin or karyorrhexis.<sup>4</sup> Acantholysis of keratinocytes has also been seen in dogs with bacterial skin infections and dermatophytosis.<sup>4</sup> Histopathology is needed to obtain a definitive diagnosis. Histopathology of the skin of a dog with pemphigus foliaceus will reveal subcorneal pustules containing neutrophils and acantholytic cells, with variable numbers of eosinophils.<sup>4</sup> Keratinocytes that have undergone apoptosis are often seen in the epidermis of dogs with pemphigus foliaceus.<sup>4</sup> Apoptotic keratinocytes are often seen in the epidermis of pemphigus foliaceus dogs and cannot be taken for bonafide markers of underlying drug reactions.<sup>4</sup> This apoptotic event may have occurred due to the rupture of desmosomal cadherin adhesion during acantholysis.<sup>4</sup> Further recommended diagnostics include a dermatophyte culture, CBC, serum chemistry panel, and urinalysis to rule out or rule in any other primary or secondary illnesses and to provide baseline bloodwork for monitoring for side effects of medications. A bacterial culture should be considered for guidance on antibiotic choices for concurrent or secondary bacterial infections.<sup>9</sup>

## **TREATMENT AND MANAGEMENT**

The treatment for the autoimmune disease pemphigus foliaceus is immunosuppressive therapy.<sup>2,4,8</sup> Immunosuppressive therapy for pemphigus foliaceus includes oral administration of a

glucocorticoid, prednisone or prednisolone, at doses ranging for 2.2-6.6 mg/kg daily depending on the weight of the dog.<sup>4</sup> Multidrug therapies are often induced with combining the prednisolone with azathioprine, cyclosporine, chlorambucil, mycophenolate mofetil, and leflunomide.<sup>4</sup> Crysotherapy, ingestion of gold salts, has been indicated as a treatment modality.<sup>6</sup> For any bacterial infections, initial treatment with cephalosporins or amoxicillin/clavulanic acid can be administered until culture results come back or for a period of 4 to 6 weeks depending on the severity of the case.<sup>8</sup> Careful consideration of drug-induced pemphigus foliaceus should be considered when selecting an antibiotic. Chlorhexidine-based shampoos may be used as well for bacterial pyoderma secondary to pemphigus foliaceus. The mainstay of the immunosuppressive therapy is to put the disease in remission and to taper the immunosuppressive medications to the least dose that controls the disease. There have been reported cases where prolonged remission has occurred after discontinuation of immunosuppressive therapy.<sup>14</sup>

### **CASE OUTCOME**

The prognosis for pemphigus foliaceus is fair to good, but lifelong therapy is usually required to maintain remission.<sup>2,8</sup> The fair to good prognosis is based from aggressive initial therapy and weaning toward remission.<sup>2</sup> During therapy, extensive monitoring of clinical signs, complete blood counts, serum biochemistry profiles, urinalyses, and urine cultures with treatment adjustments as needed are essential.<sup>8</sup>

### **CONCLUSION**

Pemphigus foliaceus is one of the most common autoimmune skin diseases seen in dogs. It also is the most common presentation of pemphigus variants. Autoimmune antibodies attack the structural proteins of the desmosomes called desmocollin-1.<sup>7</sup> Once the desmosome is attacked, the cell to cell adhesions are disrupted leading to acantholysis, which leads to blistering

and pustule formation.<sup>8</sup> Pemphigus foliaceus can affect any dog of any age or gender. It is known to most commonly affect dogs that are middle-aged. Breed dispositions include Akitas, Chow Chows, Doberman Pinschers, Dachshunds, and Newfoundlands.<sup>3,6,8</sup> There are clinical signs specific to pemphigus foliaceus. Diagnosis is confirmed by history, physical exam, cytology, biopsy, and possibly bacterial culture.<sup>2</sup> Treatment is immunosuppressive therapy with antibiotic support for secondary bacterial causes. The prognosis is fair to good in most cases; however, lifelong therapy is expected for the majority of cases.

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