Feline pemphigus foliaceous is the most common autoimmune skin disease recognized in cats and most commonly presents as a pustular, varying erosive, and crusting dermatitis. The most common locations are the face, ears, and feet (in particular, the base of the claw). Variations in the presentation include more systemic symptoms such as periareolar erosions/crusting and systemic lethargy, fever, and anorexia.

The pemphigus foliaceous variant of the pemphigus complex is caused by autoantibodies targeting a specific component of keratinocyte desmosomes. This disruption results in acantholysis (breaking up of cell-cell adhesions), resulting in separation and loss of integrity of the epidermal cell layers. When this occurs, transient pustules/blisters rupture into crusts, and scales are seen. Desmosomal proteins are expressed to different degrees depending on the anatomical site, such as the footpads and periocular skin, which is most likely the cause for the more superficial presentation of pemphigus foliaceous. Studies have confirmed the role of anti-keratinocyte IgG in cats with pemphigus foliaceous. However, different immunoreactivities suggest a different autoantigen target in cats vs. dogs.
The pustule is the primary hallmark of pemphigus; however, it can be a rare clinical presentation given how fragile they tend to be. The initial signs seen on the physical exam include serous to honey-colored crusts. Erosions, alopecia, erythema, and variable pruritus are also often seen. Most cats are affected along the pinnal margins, within the claw folds, and the periareolar and perianal regions to a lesser extent.

Cytology is the clinician's best friend in these cases, along with complete and thorough history. Pemphigus foliaceous can make this tricky in the cat, as this type of disease commonly waxes and wanes, can be rapid or very slowly progressive, and spontaneously improve. If a pustule is identified, this should be gently punctured with a needle or the corner of the slide and the slide gently pressed against the pustular contents. More commonly, the serous-seropurulent crusting should be lifted with the corner of the slide and the underlying purulent discharge pressed against the slide. The Diff-Quik method is recommended, and evaluation for acantholytic keratinocytes can be done on either high power (100x) or low power (10x). Acantholytic keratinocytes are reported in 74% of cats with pemphigus foliaceous. However, the presence of acantholytic keratinocytes is not singularly pathognomonic for pemphigus foliaceous (certain strains of *Staphylococcus pseudintermedius* and *Trichophyton* spp. dermatophytosis can also cause acanthisis). On cytology, neutrophils, eosinophils, and secondary bacterial pyodermas can also be seen.

Further diagnostics can rule out dermatophytosis based on the clinical degree of suspicion, including molecular testing (PCR), fungal culture, trichogram, or Woods lamp examination. When considering secondary bacterial pyoderma vs. primary bacterial-induced acanthisis, a combination of cytology and culture with sensitivity is typically used to start treatment. If lesions persist while the bacterial component resolves, this is a stronger indication of a likely underlying pemphigus foliaceous.

Histopathology is critical for an accurate diagnosis of pemphigus foliaceous in cats. However, the classic locations affected by this disease (pinnal margins, claw folds, generalized face) can be difficult to sample in some instances. Classic biopsy results typically display superficial epidermal and follicular pustules containing acantholytic keratinocytes without infectious organisms. These pustules typically span multiple
hair follicles and should have negative periodic acid-Schiff and Gram stains for bacteria/fungi. Eosinophils can be a prominent finding, although this tends to be seen more in systemic disease cases.

**Treatment**

Given that the primary treatment strategy of pemphigus is to induce remission and establish long-term control of the disease, the most commonly reached for initial treatment is glucocorticoids. This can be used as a sole treatment option or a combination effect with a different immunomodulatory medication. This is further discussed in the literature review section of this summary.

**Prognosis**

Recent behavioral studies (2019) of cat owners with cats diagnosed with pemphigus foliaceous indicated an overwhelmingly negative response for the time investment required to care for these patients, as well as negative financial stability and emotional wellbeing. Prognosis in these cases typically depends on both the initial response to medications and any comorbidities and side effects from initial medications. Clinical remission is higher in cats than in dogs (90% versus 50%, respectively), however cats tend to have higher chance of clinical relapse than in dogs (73% in cats versus 61% in dogs). Discussion should be had with owners regarding continuation of medications, expectations for fluctuations in this disease, and risks associated with immunomodulatory medications.

**Review in Literature**

One of the more comprehensive retrospective reviews of feline pemphigus and current recommendations is a 2019 paper from P. Bizikova and A. Burrows. They reported an original case series and previous publications for signalment, clinical features, and treatment outcome. Their original case series had 35 cats that met the inclusion criteria. All cases had acantholysis on cytological evaluation, and most cats were on average 6.8 years of age at the onset of clinical symptoms. Pustules, erosion and crusts were noted in a majority of these cats (although this was part of the inclusion criteria and therefore was required). 97% of cats had a symmetric distribution of these lesions, and 80% had two or more body regions affected. The most commonly affected skin locations were the pinnae and the claw folds, and 60% of cats showed some form of lethargy. Treatment outcomes reported no spontaneous remission, and half of the cats reported remission using glucocorticoids alone. 80% of cats were maintained with various systemic drugs with or without glucocorticoids for management, with 50% of cats maintained on ciclosporin or chlorambucil as a monotherapy.
In the literature review, 29 studies including 162 cats were selected. Acantholysis was confirmed via histopathology in 90% of cats and/or by cytology in 19% of cats. Possible drug-induced etiology was proposed in eight cats, including cimetidine, econazole/neomycin/triamcinolone/amoxicillin, itraconazole/lime sulfur doxycycline, methimazole, cefovecin, and clindamycin/carprofen. Concurrent disease association was proposed in three cats (two with a thymoma present and one with leishmaniasis). One cat developed pemphigus foliaceous post-vaccine, which resolved with immunosuppressive treatment and did not recur. Skin lesions were symmetric to a similar degree as the original case series reported in this paper (97%), with pinnae and claw folds continuing to be the most commonly affected body site. Treatment outcomes were reported in 86% of cats, with three cats reported to have spontaneous remission, and disease control was achieved in 94% of cases.

Remission was achieved typically with steroids, the most commonly selected being prednisolone. Disease control was achieved with statistically higher doses than maintenance doses, either through high steady doses of the chosen glucocorticoid or through high-dose pulse therapy (approximately 10mg/kg prednisolone/prednisolone-equivalent once daily for 3 days, then reduced to a maintenance dose of <2 mg/kg/day). No significant difference in time to disease control was noted between the pulse and standard glucocorticoid therapy. Interestingly, in the comprehensive literature review section of the paper, the median time to remission was shorter (mean 21 days) compared to the combination therapy/non-steroidal immunosuppressants as monotherapy (ranging from 29-64 days).

**Further Discussion**

Separate papers published have also assessed additional therapies. A 2021 paper by Carrasco et al. evaluated a single case report of pemphigus foliaceous in a cat treated with oclacitinib (trade name Apoquel). The presence of cardiac and renal comorbidities increased the risks associated with oral glucocorticoids; therefore, oral oclacitinib (1 mg/kg twice daily) was used with improvements seen within 7 days of initial treatments. JAK-stat inhibitors can modify lymphocyte proliferation and cytokine production (including IL-4 and IL-13), which could be involved in B-cell development and IgG antibodies.

**References**

18. Almela R, Chan, T. Review of Pemphigus Foliaceous in Dogs and Cats. Issues in Dermatology