Crusty Cats: Feline Pemphigus Foliaceus

Andrea Peterson, DVM
University of Minnesota

Lindsay McKay, DVM, DACVD*
VCA Aurora Animal Hospital
Aurora, Illinois

Abstract: Pemphigus foliaceus (PF) is an immune-mediated disease that causes pustules and crusted lesions, most commonly on the pinnae, nasal planum, periocular area, chin, and feet of affected cats. Acantholytic cells caused by degradation of intercellular adhesions are often seen on cytology but are not pathognomonic for PF. A definitive diagnosis is made based on histopathology showing subcorneal pustules with nondegenerate neutrophils and acantholytic cells. PF is treated with immunosuppressive doses of corticosteroids alone or in combination with other immunosuppressive medications, such as chlorambucil or cyclosporine. Most patients require lifelong treatment with these medications to keep the disease in remission.

Case Report
Hershey, a 6-year-old, spayed domestic shorthaired cat weighing 3.4 kg, presented with an acute onset of nonpruritic crusted lesions on the head, ears, nail beds, and nasal area. She had a 2-day history of lethargy and anorexia. She had no history of medical disease and was up-to-date on vaccinations.

Physical Examination
On presentation, Hershey was lethargic but responsive to her environment. Her temperature was elevated (103.1°F). The results of thoracic auscultation and abdominal palpation were unremarkable. She was thin, with a body condition score of 4/9, and was clinically mildly dehydrated. Other general examination findings were normal. Crusts, erosions, and scaling were present on both pinnae (FIGURE 1). Her chin had alopecia, erythema, and crusts. Additional crusts were found around her eyes, on the top of her head, on her muzzle, and in her nail beds. The nasal planum had crusting, scaling, and loss of the normal cobblestone appearance (FIGURE 2).

Diagnostic Tests
In approaching this case, there were multiple clinical signs to consider, including lethargy, anorexia, fever, loss of body condition, dehydration, and multifocal, crusted lesions. A history of acute onset of crusted lesions in cats with associated systemic clinical signs is suggestive of pemphigus
Other diagnostic differentials include bacterial folliculitis, dermatophytosis, demodicosis, pemphigus erythematosus, discoid lupus erythematosus, systemic lupus erythematosus, and cutaneous drug reaction.1 A minimum database was established for Hershey. A complete blood cell count (CBC), serum biochemistry testing, and urinalysis revealed leukocytosis with mature neutrophilia as the only abnormal finding. The level of mild dehydration was not thought to affect the results of laboratory tests. Because Hershey’s crusted lesions likely held the most diagnostic significance, cytology was conducted to assess for infection and the presence of acantholytic cells. Acantholytic cells are epithelial cells that have lost their intercellular adhesions. Samples collected from the pinnae, chin, and nail beds showed acantholytic keratinocytes, nondegenerate neutrophils, and occasional paired cocci. The cytology results were suggestive of PF and pyoderma. A skin biopsy was performed to confirm this diagnosis. Because bacterial pyoderma was evident on cytology, a tissue sample was also submitted for aerobic culture at the time of biopsy. A deep skin scraping was performed to rule out demodicosis, which can present with similar clinical signs. Skin scrapings were negative for mites. In addition, a sample was collected for fungal culture (dermatophyte test medium) because fungal disease can mimic PF in clinical signs and cytology. The results of the fungal culture were negative.

Diagnosis
Histopathology revealed pustules within the stratum corneum with a large number of acantholytic keratinocytes. An increased number of mast cells was also present within the dermis. These histopathologic findings of pustular dermatitis with acantholysis confirmed the diagnosis of PF (BOX 1). The presence of small to moderate numbers of mast cells is reported as a concurrent finding in cats with PF.2,3 Results of the culture showed Staphylococcus intermedius susceptible to all antibiotics tested, including amoxicillin–clavulanate.

Treatment
Hershey was hospitalized and given intravenous fluids (lactated Ringer’s solution, 20 mL/h over 24 hours, then 12 mL/h for an additional 24 hours) to help alleviate the fever and mild dehydration. The standard course of treatment for PF is immunosuppressive doses of glucocorticoids. Drug choices include prednisolone (initial starting dose, 2 to 8 mg/kg/d PO), triamcinolone (initial starting dose, 0.4 to 2 mg/kg/d PO), methylprednisolone (initial starting dose, 1.6 to 4.8 mg/kg/d PO), and dexamethasone (initial starting dose, 0.2 to 0.4 mg/kg/d PO).4,5 Once the lesions are in remission as determined by physical examination and cytology results, the steroids should be tapered to the lowest dose that controls clinical signs (BOX 2). Hershey was prescribed prednisolone (4.4 mg/kg/d PO) and amoxicillin–clavulanate.

Diagnosing Feline Pemphigus Foliaceus

- Transient pustules are rarely found, but erosions and yellow crusts are common.
- The face, ears, and feet are most commonly involved.
- Lesions are often localized and mild but can become generalized.
- Lesions are usually bilaterally symmetric.
- Impression smears show acantholytic cells and neutrophils.
- Secondary infections are common.
- Definitive diagnosis is based on histopathology.

Tapering Steroids

- Daily dosing is required until clinical signs resolve, which often takes 2 to 4 weeks. If remission is not achieved after this time period, consider either an alternative steroid (triamcinolone, dexamethasone, or methylprednisolone) or additional immunosuppressive medication (chlorambucil or cyclosporine).
- Once clinical signs have resolved, transition to every-other-day dosing by decreasing the every-other-day dose by 25% every 2 to 4 weeks. For example, if the starting dose is 10 mg/d of prednisolone, taper to 10 mg alternating with 7.5 mg every other day. Continue to recheck the cat every 2 weeks. If remission continues, taper to 10 mg alternating with 5 mg, and so on, until the cat is receiving 10 mg every other day.
- Once the cat is on every-other-day dosing of prednisolone, lower the dose by 25% every 4 to 6 weeks. For example, taper from 10 mg every other day to 7.5 mg every other day.
- Slowly decrease the dose to the lowest amount that controls clinical signs. Maintenance dosing of prednisolone is generally about 0.5 to 1 mg/kg every other day. Tapering and maintenance doses of methylprednisolone are similar to those of prednisolone.
- Tapering of dexamethasone or triamcinolone is performed similarly to that for prednisolone; however, maintenance dosing is generally about 0.1 to 0.2 mg/kg q48–72h for triamcinolone and 0.05 to 0.1 mg/kg q48–72h for dexamethasone.

Box 1: Diagnosing Feline Pemphigus Foliaceus

Box 2: Tapering Steroids
clavulanate (18.4 mg/kg bid PO). She was rechecked every 2 to 4 weeks over the following 6 months, and the steroids were slowly tapered to maintenance doses of 1 mg/kg of prednisolone every other day. The amoxicillin–clavulanate was discontinued after 4 weeks when cytology and physical examination showed resolution of the pyoderma.

Hershey has been stable on maintenance doses of prednisolone for the past 2 years. Now that she is stable on maintenance therapy, rechecks are performed every 6 months to assess her PF as well as monitor for possible adverse effects of chronic prednisolone use. This schedule ensures that the PF is well controlled. Laboratory monitoring of cats receiving long-term glucocorticoids includes a CBC, serum biochemistry testing, and urinalysis.

**Overview of Feline Pemphigus Foliaceus**

PF is an immune-mediated disease affecting the superficial epidermis. The pathogenesis has been well documented in humans and dogs, and feline PF is hypothesized to have a similar disease process. In dogs and humans, autoantibodies are produced against keratinocyte intercellular adhesions called desmosomes. These autoantibodies bind to desmosomes and cause the conversion of plasminogen to plasmin via proteolytic enzymes. Plasmin released directly to acantholysis. The ultimate loss of these intracellular adhesions leads to the formation of acantholytic cells. In cats, neutrophilic inflammation occurs with the formation of acantholytic cells, leading to pustule formation.

Although PF is a rare disease, it is the most common immune-mediated dermatologic condition in cats. There is no known sex or breed predisposition, and the average age at onset is 5 years. The cause of PF is often idiopathic, but drug reactions to medications, including potentiated sulfonamides, amoxicillin, cimetidine, and vaccines, have been reported.

Cats with PF present with hemorrhagic or serous crusts, scaling, alopecia, and erosions. Intact pustules are transient and rarely detected. Lesions are frequently localized to the pinnae, nasal planum, periocular area, chin, and nail beds but can generalize to involve the ventral and dorsal thoracic areas. The lesions are often bilateral and symmetric, and they can be pruritic. Systemic clinical signs such as lethargy, anorexia, dehydration, and fever can be present. The CBC may be normal or nonspecific with neutrophilia or eosinophilia. Serum biochemistry results are often normal or have nonspecific abnormalities. Impression smears of affected pustular or crusted areas should be obtained. Cytology typically reveals acantholytic cells with nondegenerate neutrophils. However, acantholytic cells are not pathognomonic for PF. They can also be seen in cases of dermatophytosis, severe bacterial infection, or pemphigus erythematosus. Bacteria may also be seen if secondary pyoderma is present.

Histopathology is required for a definitive diagnosis. It is best to biopsy a pustule; however, these are rarely seen. Crusts are most often biopsied if no pustules are present. Biopsy sites should not be clipped or scrubbed, and the crust should remain attached to the underlying skin. Three or four biopsy samples should be taken to give the best chance of making the diagnosis. Ideally, oral glucocorticoids should be discontinued for 2 to 3 weeks before sample collection, and injectable glucocorticoids should be discontinued for 6 to 8 weeks. Samples collected from active lesions (i.e., pustules or crusts) demonstrate subcorneal pustules with neutrophils and acantholytic cells. An increased number of eosinophils and/or mast cells may also be present.

Treatment generally begins with immunosuppressive doses of glucocorticoids. Prednisolone is often a good starting drug because its absorption and activity in cats are greater than those of prednisone. Prednisolone (2 to 8 mg/kg PO) is given daily until remission is achieved. After lesions are resolved (approximately 2 to 8 weeks of daily dosing), a slow tapering course to maintenance dosing is started. If clinical signs return during the tapering period, the dose must be increased to a level that maintains remission. If remission is not obtained with prednisolone at the initial starting dose or a relapse is noted with tapering, the dose can be increased. However, higher doses of prednisolone (>4 mg/kg/d) and prolonged periods (>4 weeks) on high daily doses of steroids carry the risk of increased adverse effects. In general, cats

---

**BOX 3**

**Improving Dermatohistopathology Results**

- Discontinue oral steroids 2 to 3 weeks before biopsy.
- Discontinue repository steroids 6 to 8 weeks before biopsy.
- Treat secondary infections before biopsy.
- Select areas with active lesions, especially pustules and crusts.
- Select three or four areas for sample collection.
- Do not prepare the area (i.e., do not clip or scrub)
- Use a large punch size (i.e., 6-mm biopsy punch).
- Attempt to keep crusts and scales attached.
- Provide pathologist with history, physical examination findings, laboratory findings, treatment, and differential diagnosis.
are more resistant than dogs to the adverse effects of glucocorticoids. Polyuria, polydipsia, polyphagia, depression, and diarrhea are the most common clinical signs. Urinary tract infections are also seen due to low urine specific gravity and immunosuppression. With long-term glucocorticoid use, cats can also develop diabetes mellitus; this is more common in cats that are already genetically predisposed. In addition, cats that are obese, are on a high-carbohydrate diet, or have concurrent hormonal disease are also predisposed to developing diabetes. CBCs, serum biochemistry testing, and urinalyses are part of routine monitoring for adverse effects of glucocorticoid therapy. We recommend performing these tests every 4 to 6 weeks for the first 3 months and then every 6 months thereafter.

If the patient experiences adverse effects from prednisolone, an option is to change to an alternative glucocorticoid such as triamcinolone (0.4 to 2 mg/kg/d PO), methylprednisolone (1.6 to 4.8 mg/kg/d PO), or dexamethasone (0.2 to 0.4 mg/kg/d PO). If additional immunosuppression is required or the cat is experiencing excessive adverse effects from the steroids and a steroid-sparing therapy is needed, chlorambucil (0.1 to 0.2 mg/kg/d PO) can be added (FIGURE 3). In addition, a more current treatment is to use cyclosporine (5 to 10 mg/kg/d PO) in cats with PF. Anecdotal reports suggest that cyclosporine leads to good control of PF and supports its use. If a good clinical response to medication is seen, the cyclosporine frequency of administration can be decreased, with a goal of eventually discontinuing the medication. Discontinuation is not feasible in most cats because clinical signs recur during tapering; therefore, these cats are continued on maintenance doses of immunosuppressive medication.

Adverse effects of chlorambucil include myelosuppression (anemia, panleukopenia, thrombocytopenia) and gastrointestinal toxicity (anorexia, vomiting, diarrhea). These effects are gradual; bone marrow suppression occurs with a nadir at day 7 to 14 and recovery at day 14 to 28. If chlorambucil is prescribed, a CBC should be checked every 1 to 2 weeks for the first 3 months and every 6 months thereafter. If severe adverse effects occur, chlorambucil should be discontinued and other therapies investigated. Common adverse effects of cyclosporine include gastrointestinal upset, most often diarrhea or soft stool. Rarely, acute toxoplasmosis has been reported as an adverse effect of cyclosporine use in cats. Long-term monitoring is also recommended in cats receiving cyclosporine (CBC and biochemistry testing every 4 to 6 months). If adverse effects are encountered, the cyclosporine dose should be decreased or discontinued, based on the severity of the effects.

Many cats with PF have concurrent pyoderma, and S. intermedius is the most commonly isolated bacterial species. Systemic antibiotics such as amoxicillin–clavulanate or cephalosporins (e.g., cefadroxil) are generally effective. The prognosis for patients with PF is fair to good, depending on the ease of achieving remission and the tolerance of therapy. Some patients are able to maintain lifelong remission without steroids, but most require long-term immunosuppressive therapy. In some cases of drug-induced PF, glucocorticoids can eventually be discontinued.

References