Allergy Mimickers

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When a clinician is presented with a pruritic patient, it is correct to initially consider, and rule out, the more common hypersensitivity disorders. Atopic dermatitis, adverse food reactions, and parasite hypersensitivities (especially flea allergy dermatitis) are seen on a daily basis. The challenge is to not overlook other dermatological conditions which might cause pruritus. An overview of some of the "allergy mimickers" will be presented with emphasis on specific clinical changes which should alert the clinician to consider these mimickers.

Four common conditions misdiagnosed as allergic skin disease are sebaceous adenitis, folliculitis (specifically demodicosis and dermatophytosis), cutaneous epitheliotropic T cell lymphoma and pemphigus foliaceus

Sebaceous adenitis (SA) is an inflammatory disease of the sebaceous glands which can lead to their destruction. An inheritance mode is suspected, especially in breeds such as the Standard Poodle. Breeds predisposed for development include the Akita, Standard poodle, Vizsla, Samoyed, German shepherd and Havanese. However SA is seen in many other breeds, as well as mixed breeds.

When sebaceous glands are damaged or destroyed by SA, resulting changes are predicable. Lesions include alopecia (patchy or generalized), scale and dry skin, follicular cast formation, variable amounts of erythema, and nodule or plaque formation in some patients. Occasionally the affected skin and hair will become discolored or hyperpigmented. Bacterial pyoderma is common in these patients as sebum from sebaceous glands is important for both barrier function of the epidermis and for the bactericidal properties.

Sebaceous adenitis is misdiagnosed as allergic skin because these patients can be pruritic, both because of the actual disease, and also because of the concurrent secondary infections. Keys to help distinguish SA from allergic disease is the amount of scale tends to be greater in SA, as well as the alopecia tends to be more dramatic compared to allergic skin. The skin is actually dry (hypohidrosis) where as in most allergic patients there is often increased amounts of sebum. Remember that scaly skin is not necessarily dry skin. Because the alopecia can be generalized and bilaterally symmetrical, SA can also be misdiagnosed an endocrine disorder. Finally, the presence of follicular casts are very suggestive of SA and warrants biopsy. Sebaceous adenitis is confirmed with histopathology.

Therapy basically attempts to replace sebum and its function, as well as potentially allow regeneration of sebaceous glands. Supportive care of the skin includes anti-seborrhea baths and rinses. If the shampoo also contains chlorhexidine, antibacterial benefits will be achieved which could reduce the need for systemic antibiotics. New products such as ceramides or phytosphingosine act as the mortar of a brick wall which improves barrier function and improves clinical signs. Concurrent therapy with Vitamin A (600-1,000 IU/kg daily) and omega 3/6 fatty acid supplementation are also encouraged. Baby oil (or other oils) applied to the skin as a "soak' for 30-60 minutes are labor intensive, but many owners are pleased with the results. The oil is washed off with a gentle shampoo after the soak. Topical humectants such as Propylene glycol, urea, lactic acid, glycerin (Humilac™) can be applied daily or as desired by the owner. Cyclosporin (5-10 mg/kg daily) has been shown to cause improvement of clinical signs and there is documentation that sebaceous glands can regenerate when patients are receiving cyclosporin therapy. In my experience complete control or "cures" are uncommon, and balancing the therapy with clinical signs, patient comfort, and cost is the goal and challenge for the owner and clinician.

Other conditions which mimic allergic skin disease are two causes of folliculitis, namely Demodex and dermatophytosis.

Demodicosis is infestation by Demodex mites. In addition to D. canis, several additional Demodex mites have been described in the dog and include the large bodied D. injai which lives in sebaceous glands and the short-bodied D. cornei which is found in the superficial epidermis. Demodex injai is only present in low numbers and is associated more with a greasy or oily dermatitis on the dorsal neck and trunk. Because all species of Demodex can cause inflammation and subsequent pruritus, patients with Demodex are misdiagnosed as suffering from atopic dermatitis or other allergic diseases. The obvious and simple way to prevent this is to "Always Scrape."

Clinical signs of demodicosis include alopecia, erythema, papules, comedone formation and potentially deeper bullae, fistulous tracts and pustules when secondary pyoderma develop. Serous and or hemorrhagic crust can also be present. With the follicular species, a subtle dark "sheen" may develop due to follicular plugging (less dramatic than a comedone). Two locations where demodex mites tend to be overlooked are when present in the feet or ears. When localized in the feet, a pruritic pododermatitis can develop which is frequently misclassified as allergic disease. Demodex mites can cause a dramatic ceruminous otitis and if patchy alopecia is not present elsewhere, the diagnosis is easily overlooked.

Diagnosis is usually made with skin scrapings. Shaving the hair, placing mineral oil on the site to be scraped, and gently squeezing the skin to promote extrusion of the mites to the surface can all enhance recovery of mites. In areas such as interdigital folds where it is difficult to scrape effectively, plucking hair and placing on a slide with mineral oil may yield mites. Swabbing or scraping ceruminous material from the ear pinnae and placing in mineral oil is also indicated. Numerous treatment options are now available and are beyond the scope of these notes to discuss.

Dermatophytosis is the second cause of folliculitis which will occasionally present with significant pruritus and be misdiagnosed. The three species of dermatophytes commonly diagnosed in dogs and cats are Microsporum canis, M. gypseum and Trichophyton mentagrophytes with the latter being able to cause the most inflammation and most likely to mimic allergic skin disease.

Clinical signs include patchy or generalized alopecia, erythema and scale. The diagnosis is best made with fungal (DTM) cultures of the skin and hair. The toothbrush technique will increase the sensitivity of the testing. Remember Trichophyton species can be slower growing the Microsporum which is why we always hold our cultures a minimum of three weeks. Trichophyton may form macroconidia in low numbers which can make the correct speciation of the fungus difficult. In such cases if the color of the colony remains light (white, light tan or yellowish) it may be prudent to submit the culture to a commercial laboratory. Because treatment may require many months it is especially prudent the diagnosis be made correctly. Treatment involves both topical and systemic antifungal medications and is beyond the scope of these lecture notes.

Cutaneous epitheliotropic T-cell lymphoma (CETL) or mycosis fungoides is defined as a spontaneous neoplasm of skin and mucous membranes in which neoplastic T lymphocytes infiltrate the epidermis and adnexal structures. The average age at onset is 9-11 years which should be the first clue when trying to distinguish from allergic disease. Several clinical forms or manifestations will occur in the dog and include an exfoliative erythroderma, plaques and nodules, ulcers or erythema of the oral mucosa and mucocutaneous lesions. An exfoliative erythroderma is defined as erythematous scaly skin along with alopecia and potential hypopigmentation. The pruritus can be variable but up to 50% of the patients with a CETL are pruritic which is why it is misdiagnosed as allergic disease.

Clinically because this is a neoplastic disorder there are often subtle (and not so subtle) physical changes of the skin which should raise the index of suspicion regarding CETL. The size of the scale itself is different with CETL. The scale is larger, even to the point of being described as “sheets” of scale and also appears more “shiny.” Many patients with CETL will exhibit hypopigmentation which would be unusual in allergic disease. Distribution of lesions can also be helpful. In some reports, up to 50% of patients had involvement of the mucosa. Foot pad lesions are not uncommon with CETL whereas in allergic disease the footpad is usually sparred (although interdigital skin is certainly affected with allergic disease). Patients with CETL may also develop plaques or nodules in the skin which would be unusual for allergic disease. Finally with close scrutiny the skin itself (even hypopigmented skin) reveals subtle thickening or swelling suggesting an infiltration process.

Diagnosis is based on histopathology although cytology of lesions will sometimes reveal numerous lymphocytes which raise the index of suspicion for CETL and further mandate biopsies. Biopsies of scale, plaques, hypopigmentation or significantly erythematous lesions are the best for sampling.

There are conflicting reports regarding correlation of chronic inflammatory skin disease with the development of CETL. Santoro et al (Vet Derm 2007) found that atopic dogs were 12 times more likely to develop CETL, however Fontaine et al (Vet Derm 2010) found no association between CETL and previous chronic dermatosis. The long-term prognosis of CETL is poor with an average survival time of six months after the diagnosis is made. Treatment is not known to extend the survival rate, but is known to improve the quality of life. Corticosteroids and lomustine are two of the drugs of choice when treating CETL but consultation with an oncologist is suggested, especially if the clinician is not familiar with the use of lomustine.

Pemphigus foliaceus (PF) is one of the most common autoimmune skin diseases of dogs and cats and is the final allergy mimicker which can be misdiagnosed as allergic disease. Pemphigus is a bullous autoimmune skin disease that affects the epidermis and hair follicles. In dogs and cats, 5 forms of pemphigus have been recognized: Pemphigus foliaceus, pemphigus erythematosus, panepidermal pustular pemphigus, pemphigus vulgaris, and paraneoplastic pemphigus. Pemphigus foliaceus is the most common form and may be further divided into spontaneous forms and drug induced PF.

In dogs, breeds such as the Akita, Chow Chow, Doberman pincher, schipperke and others are predisposed to the development of spontaneous PF. Some of the drugs implicated in triggering drug-induced PF in humans include the Thiol compounds and sulph-hydryl (-SH) groups. In dogs, some of the drugs more commonly linked to a drug eruption include Trimethoprim/sulfonamides, other antibiotics such as penicillins and cephalosporins, Rifampin, captopril, enalapril, piroxicam, phenylbutazone, and phenobarbital. Doberman pinchers and Labrador retrievers may be predisposed to drug induced pemphigus foliaceus.

Cats can be especially challenging to make a correct diagnosis if pemphigus foliaceus. Pustules are not always as obvious or as stable (they quickly dry into crust). Crust on the dorsal nasal area, pinnae, digits (paronychia) and nipples or areola area should always prompt the clinician to consider PF and perform appropriate diagnostic tests to confirm or rule out this possibility.

The hallmark lesion of PF is a pustule which may be larger (bullous) and not necessarily centered around hair follicles. Because pruritus can also be present, these patients are frequently “assumed” to be allergic with a secondary pyoderma. If treated with anti-inflammatory doses of corticosteroids the disease can be partially subdued but not ideally controlled due to insufficient dose. The “classic” presentation of PF is for pustules to develop on the nasal planum, as well as the nasal bridge, pinnae, and then become generalized from there. When patients do not have the facial distribution of lesions, the disease is more likely to be overlooked or missed. The development of pustules can wax and wane (or “come in waves”) and concurrent pruritus can be variable but may be intense. Affected patients may also be anorexic, febrile, lethargic, and may present with lameness if the footpads are affected.

The diagnosis is based on microscopic evidence. Cytology is helpful in distinguishing PF from a superficial pyoderma. The presence of acantholytic cells and absence of bacteria from cytology samples can help raise the index of suspicion regarding PF but confirmation should be based on histopathology of an intact pustule. If pustules are not present for sampling, then biopsy of crust can be diagnostic, but care should be taken to leave the crust attached to the underlying epidermis.

When treating a patient with PF the primary goal is to balance the drugs with their efficacy, cost, and tolerance (side effects) by the patient. The goal is not necessarily to prevent every pustule from forming. Corticosteroids are the mainstay of therapy for PF, but better control of the disease can be achieved when multiple different drugs are used, and it is possible to see synergistic effects between the drugs. Azathioprine and cyclosporine are two systemic drugs often combined with the steroid. Once control is achieved, the clinician should start to reduce the medication, and this will partially be based on any side effects from the drugs being used. Regular monitoring of a CBC and chemistry panel will be necessary. Most patients will start to improve and allow a reduction in dose after 2-4 weeks of initial therapy. Gentle shampoo therapy may be useful in crust removal, but caution owners to avoid intensive scrubbing of the skin.

The prognosis is variable, but most cases with PF respond reasonably well to therapy, especially when multiple therapies are utilized so that the corticosteroids can be minimized. Patients should be rechecked at least two times/year and monitoring parameters include physical exam, clinical signs, secondary skin infections, CBC, chemistry panel, urinalysis, urine culture and sensitivity. Long-term treatment is usually required, however some patients may remain in remission and discontinuing immunosuppressive therapy is a possibility. Long-term immunosuppressive therapy may lead to recurrent pyoderma, demodicosis, or dermatophytosis, which are more reasons to try and find the minimal amount of drug therapy necessary for acceptable control of the disease.