Proceeding of the ACVP Annual Meeting

Oct. 17-21, 2015
Minneapolis, MN, USA

Next Meeting:
Dec. 3-7, 2016 - New Orleans, LA, USA

Reprinted in the IVIS website with the permission of the ACVP
Introduction
Science in Veterinary Dermatology has rapidly accelerated in past two decades and much of the mantra ingrained in textbooks has come into question. The challenge for the diagnostic pathologist is how to keep up with literature in order to communicate with clinicians and deliver the best possible biopsy interpretation. Keeping in mind that skin has a limited means to react to injury, one must be aware of subtle, often breed specific, histologic changes and their clinical correlations. Furthermore, many disorders are clinical, not histologic, diagnoses. In skin biopsy analysis, the job of the pathologist is to assist with care of the animal and not always to achieve a diagnosis. This lecture is focused on changes in the literature that may impact the interpretation of a skin biopsy. Some of the material is the sole opinion of the author.

Getting Started:
For dermpath newbies, approach a skin case the same way you are trained to review other organs (i.e. use a standard system to assess all skin components- epidermis, basement membrane zone, superficial and deep dermis, adnexa, vasculature, subcutis). Always analyze the slide before you read the history; read the history and look at the slide again. Know species and breed differences in normal skin anatomy.

Pattern Analysis
The accepted practice in dermatopathology is slide analysis by pattern diagnosis. For each pattern below, paradigm shifts or new entities will be discussed.

Perivascular dermatitis
This is the most frustrating and common histologic diagnosis. I estimate 40% of my inflammatory skin biopsies have some form of “pv dermatitis” in the morphologic diagnosis. As patterns go, this pattern has very little diagnostic weight.

1) Allergic skin disease nomenclature:
Make sure you have eliminated the term “allergic inhalant dermatitis” from your reports. This term was ousted from the veterinary profession in 1999 due to absence of asthma in atopic dogs, an inability to cause skin lesions in dogs sensitized via inhalation and because spontaneous atopic dermatitis (AD) resembles contact dermatitis[1]. The term “cutaneous adverse food reaction” has replaced “food allergy” and “food hypersensitivity” because the pathologic
mechanisms are usually unknown. Is the reaction a specific immune-mediated response (e.g. Type I hypersensitivity) to food antigens or a nonimmune-mediated intolerance to a component in the food? Canine adverse food reactions can trigger gastrointestinal disturbances as well as flares of atopic dermatitis. Furthermore, food induced atopic dermatitis and nonfood induced atopic dermatitis are clinically indistinguishable[2].

2) Allergy theory: In contrast to “allergic inhalant dermatitis” or “inside out theory”, new research supports the “outside in” theory in regard to sensitization in atopic dermatitis. An abnormal skin barrier (stratum corneum) allows for allergen penetration and sensitization. There is reasonable evidence that dogs with AD have an altered skin barrier: deranged lipid profiles in the SC (e.g. decreased free ceramides), ultrastructural change in SC of atopic dogs and increased transepidermal water loss (TEWL) in both normal and abnormal skin[3].

2) Allergy diagnosis:
Pathologists should be aware of the common gross manifestations of allergic skin disease in all domestic animals. Do not try to distinguish atopy, adverse food reaction and ectoparasite hypersensitivity on a skin biopsy unless you see bugs (e.g. scabies mites). Yes, there may be subtle histologic hints (i.e. eosinophilic nibbles in flea bite hypersensitivity), but the clinical manifestations (signalment, pattern, location, type of lesion) are much more powerful. Atopic dermatitis is a clinical diagnosis based on detailed clinical parameters that have been the subject of much review and recent validation[2, 4, 5].

Do not use “allergy” as your default diagnosis. If a feline pemphigus foliaceus case lacks surface crusts (i.e. location of acantholytic cells), the cutaneous reaction pattern may appear “allergic” (i.e. eosinophilic and mastocytic inflammation). The clinical features provided by the clinician will help you avoid this mistake. Ask for the clinical description if not included in the history. Also avoid using “allergic dermatitis” as your morphologic diagnosis. Use the comment to say the histologic changes support the clinician’s diagnosis of allergic skin disease.

**Intraepidermal pustular/vesicular dermatitis**

1) Superficial pemphigus (pemphigus foliaceus- PF) remains the most common autoimmune skin disease in domestic animals. The diagnosis is usually straightforward and still driven by histopathology alone. It is now known that the major antigen is Desmocollin-1. In contrast to humans, desmoglein 1 is only a minor autoantigen in dogs[6].

2) Pemphigus erythematosus and pemphigus vegetans are terms that have been loosely applied to veterinary diseases based on human comparisons. Except for the rare exception, these diagnoses most likely represent variations of PF. There
is one case report of well-documented pemphigus vegetans that resembles the human counterpart[7]. Panepidermal pustular pemphigus is also deep epidermal form of PF. Pemphigus erythematosus maybe regarded as facially-localized PF[8].

3) Be careful to assess for dermatophytes in suspected PF cases, particularly those with folliculitis and minimal to mild acantholysis.

4) You should also be aware of topical drug induced PF cases and always consider a topical PF reaction when the lesions are localized on the dorsum (i.e. site of application of product[9, 10].

Interface dermatitis

1) While this is a powerful histologic pattern (i.e. few differential diagnoses), the question is always is it interface or not? Many of the true interface diseases have strong breed and site predilections. Discoid lupus versus mucocutaneous pyoderma is the most difficult[11]. Nasal planum biopsies are notoriously difficult and equally despised by most pathologists. Client education is important here and if the clinical presentation is classic for DLE (depigmentation, loss of cobblestone architecture, ulcer/crusts), the dog probably doesn’t require a biopsy at all. In contrast to DLE, MCP affects the margins of nonhaired skin and adjacent haired skin (i.e. planum, lips). Stress that the purpose of the biopsy is to rule out other diseases (epitheliotropic lymphoma, superficial pemphigus, VKH and superficial dermatophytosis). If you are forced (and don’t be) to give treatment advice, most DLE cases respond to immunomodulatory agents and do not require corticosteroids.

3) SLE is not a good differential diagnosis for a cutaneous interface reaction. Cases of only SLE in domestic animals that have a cutaneous lupus specific reaction are exceedingly rare. Furthermore, cutaneous lupus (e.g. vesicular lupus, localized and generalized discoid lupus) does not progress to SLE. A new form of lupus in dogs was recently reported (mucocutaneous lupus)[12].

4) There is literature discrepancy for the histologic diagnosis of the erythema multiforme/Stevens Johnson syndrome and toxic epidermal necrolysis spectrum. In short, the diseases are separated by the clinical (not histologic) manifestations (i.e. type of lesion, lesion distribution and extent and degree of mucosal involvement). Furthermore the EM in dogs is not equivalent to “EM” in people. The reader is referred to the exceptional review article by J. Yager[13].

Subepidermal vesicular dermatitis

1) For congenital blistering disorders, epitheliogenesis imperfecta and aplasia cutis congenital are outdated terms in companion animals and will now fall into categorization of epidermolysis bullosa (EB). EB is further divided into three
subgroups based on the site of defect in relation to the basal keratinocyte/basement membrane zone (EB simplex, Junctional EB, Dystrophic EB).

2) In the **acquired blistering disorders**, bullous pemphigoid is a reasonable differential diagnosis for horses but not for dogs and cats. Cases reported as bullous pemphigoid were cited before techniques were available to identify the target protein. Furthermore, most cases in dogs and cats would now be classified as mucous membrane pemphigoid[14].

**Folliculitis/Furunculosis**

Post grooming furunculosis is a type of acute hemorrhagic and necrotizing folliculitis that has been associated with contaminated grooming products. The rupture occurs in the upper infundibulum. The dogs present with dorsally oriented hemorrhagic crusts and erythematous papules +/- fever and lethargy. The lesions are painful and may be confused with other diseases (e.g. discospondylitis)[15].

**Nodular/Diffuse dermatitis**

The histiocytic diseases have become even more complicated with the recognition of inflamed lymphoma in dogs. This disorder is very difficult to differentiate from cutaneous reactive histiocytosis on light microscopy and it has a less favorable prognosis[16] .

**Vasculitis**

Remains a difficult and often controversial diagnosis. In small breed dogs, the vaccine associated “ischemic dermatopathy” subjectively appears to increasing and more likely to involve distal extremities and nontraditional breeds (i.e. large breed dogs rather the miniature poodle/bichon/Chihuahua).

**Miscellaneous**

1) **Primary seborrhea** is another outdated term that originated in 1960s and early 70s long before the impact of *Staphylococcus* and *Malassezia* were known. Cases of so-called primary seborrhea would likely be classified today as any of the following: sebaceous adenitis, vitamin A responsive dermatosis, ichthyosis, *Malassezia* dermatitis, etc.[17].

2) Do not give treatment advice. Some diagnostic labs have canned comments with drug dosages. These are often wrong, not up to date, or completely inappropriate for the health of the animal. Make the clinicians do their own work or let the consulting dermatologist give a drug dose if requested.
3) Historical information on antimicrobial administration has to be interpreted with caution. While it is useful to know that the animal failed to respond to appropriate antibiotic treatment, there has been a surge of MDR S. pseudintermedius and S. scheiferi in superficial pyoderma. The failure to respond to antimicrobial therapy does not help you histologically distinguish PF from superficial pyoderma.

References:


