Abbey Veterinary Services
DIAGNOSTIC HISTOPATHOLOGY AND CYTOLOGY

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CASE OF INTEREST

A case of pemphigus vulgaris in a dog.

By Richard Fox, Veterinary Pathologist

A 7 year old male entire Labrador presented with rapid onset multifocal to coalescing areas of ulceration affecting nasal planum, prepuce, lips, gingiva, soft and hard palate. Paroxsysmal sneezing was also noted. Nasal flushes were performed but no signicant changes were noted on rhinoscopy and cytological examination. Autoimmune disease was suspected clinically and biopsies were taken from preputial, nasal plamun and oral cavity.

Three sections of tissue were examined, one identified oral mucosa, the other two haired skin. Two of the cutaneous lesions displayed ulceration but in the oral mucosal biopsy there was suprabasilar clefting of the mucosal epithelium.

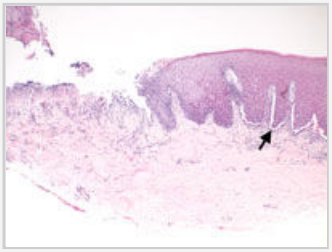

Figure 1. Histological section of the oral biopsy displaying an ulcer and bordering mucosal epithelium with conditioned suprabasal clefting. HE Stain.

This also was present, as a conditioned artefact, in one piece of haired skin which affected hair follicles.

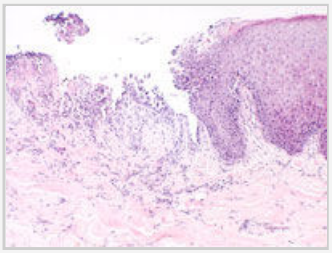

Figure 2. Histological section showing tombstoning of residual basal cells with acantholysis. HE Stain.

Occasional neutrophils were present in the cleft and there was also evidence of mild acantholysis in the areas of clefting. Areas of ulceration were evident adjacent to the areas of clefting.

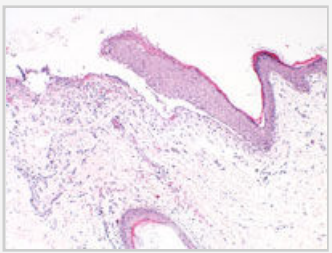

Figure 3. Histological section of haired skin showing further suprabasilar epidermal clefting and ulceration. HE Stain.

A diagnosis of pemphigus vulgaris was made on the clinical and histopatholgical findings.

Pemphigus vulgaris (PV) is a very rare, severe vesicobullous and ulcerative autoimmune disease reported in the dog and cat. Desmoglein 3 (Dsg3), an adhesion molecule (cadherin) of keratinocytes, is more strongly expressed in the suprabasilar kerarinocytes of the oral mucosa, and has been identified as the targeted antigen in canine PV, as occurs in humans). However, when lesions of PV affect the haired skin as well as mucous membranes, other antigens such as destmoglein 1 (Dsgl), which is more strongly expressed in superficial keratinocytes of haired skin, may be targeted.

Drug-induced PV may occur in humans; removal of the offending drug leads to reversal of the lesions (Brenner er al., 1998). PV-like skin reactions putatively due to drug therapy (including sulfasalazine) have been observed sporadically in both dogs and cats. Also, transient, often orally confined, cases not explained by adverse drug reactions have been seen by the authors in these species.

The exact pathomechanism of vesicle and bulla formation is not known. Autoantibodies have been found but do not on their own give rise to lesions and investigation is ongoing.

In this issue:

JOURNAL Articles(with e-links)

1. Sabattini S, Bettini G. Prognostic value of histologic and immunohistochemical features in feline cutaneous mast cell tumor.s Vet Pathol. 2010 Jul;47(4):643-53. Link

Feline cutaneous mast cell tumors (MCTs) have been histologically classified as mastocytic (well differentiated or pleomorphic) and atypical/poorly granulated. Their biologic behavior ranges from benign to malignant, but prognostic factors are not well defined. Histologic classification, number of tumors, mitotic index, cytoplasmic granularity, and infiltration by eosinophils or lymphocytes were evaluated retrospectively in 25 feline cutaneous MCTs. Immunohistochemistry was applied to assess KIT (CD117) pattern and immunoreactivity score, telomerase expression (human telomerase reverse transcriptase), and proliferation index (MIB-1/Ki67 index). Case outcome was obtained via telephone interviews. The tumors comprised 15 mastocytic well-differentiated, 7 mastocytic pleomorphic, and 3 atypical/poorly granulated MCTs. Immunohistochemically, CD117 was expressed in 13 of 25 tumors (52%), and telomerase reverse transcriptase was expressed in 15 of 22 (68%), with no correlation to histologic classification. Mitotic index, KIT immunoreactivity score, and Ki67 index were significantly higher in mastocytic pleomorphic MCTs than in the other 2 categories. Five cats (20%) died of tumor-related causes. Multiplicity of lesions, pleomorphic phenotype, KIT immunoreactivity score, and mitotic and Ki67-indices correlated with an unfavorable outcome. Mitotic index was the strongest predictive variable. These results suggest that histologic classification, CD117/KIT immunohistochemistry, and proliferation indices may help to identify potentially aggressive cases of feline cutaneous MCT. Aberrant KIT protein localization and telomerase immunoreactivity warrant further exploration as potential prognostic markers.

2. Schobert CS, Labelle P, Dubielzig RR. Feline conjunctival melanoma: histopathological characteristics and clinical outcomes. Vet Ophthalmol. 2010 Jan;13(1):43-6. Link

A report on the histopathology and clinical features of 21 cases of feline conjunctival melanoma.
A total of 18 cases are from the COPLOW collection and three cases from Antech Diagnostics. We tabulated the location of the tumor, pigmentation, cell shape, mitotic index and presence of multinucleated tumor cells. Surveys were sent to referring ophthalmologists to obtain further information about each case.
The mean age of the cats was 12.4 years. A total of 11 cases were neutered males, six spayed females, and one each of intact female and male. Thirteen of the 21 cases were located on the bulbar conjunctiva, three on third eyelid only, three on palpebral conjunctiva. Sixteen tumors were pigmented while five were amelanotic. Seventeen of the cases consisted of round cell only while four cases were mixed populations of round and spindle cell. Fourteen of the cases contained

Histologically the suprabasilar acantholysis creates fragile, transient vesices and bullae that rapidly progress to ulcers. Partial bilateral symmetry, especially facial, can be striking. Fragile, irregularly shaped vesicles and bullae develop in groups. Erythema may precede vesicle formation, especially in haired skin areas (Olivry, 2003). Rupture of vesicles and bullae rapidly leads to erosions; secondary surface bacterial overgrowth then results in widespread ulceration. Crusting is a feature of nonmucosal ulcerations. Ulcers expand, creating lesions that are substantially larger than the previously existent intact bullae. These ulcers are irregularly shaped and may coalesce further. A positive Nikolsky sign (the artificial extension of a blister or ulcer induced by digital pressure to adjacent mucous memhrane or skin) may be elicited.

Most dogs and cats have lesions affecting the oral cavity and muucocutaneous junctions. Coalescing ulcers on the tongue palate, and gingiva which are not contiguous with the teeth should increase clinical suspicion for PV. Lip involvement usually is seen with extensive oral disease. Thick, ropy, tenacious, odorous saliva is an additional feature.

Most dogs that develop PV are adult or aged. In contrast to bullous pemphigoid, the ulcers 0f PV coalesce and expand, leading to lesions that are substantially larger than previously existent intact bullae. Histopathology should allow differentiation.

Intact vesicles or margins of recent ulcers should be removed for biopsy. The typical lesion of PV is a suprahasilar cleft or separation due to acantholysis, leading to formation of a bulla. Often the roof of the hulla detaches from a specimen, leaving a row of basal cells attached to the basement membrane. This row of plump or rounded basal cells, commonly called 'tombstone' cells, remains at the base of the cleft. Active acantholysis may be seen above the cleft, and free acantholytic cells may be present within the lumen.

The most current commonly used therapeutics include glucocorticoids, azathioprine, chlorambucil and tetracycline and niacinamide but current alternative therapeutics include cyclosporin and tacrolimus, mycophenolate mofetil and additional alternative therapeutics include cyclophosphamide, chrysotherapy, dapsone, sulfasalazine and intravenous immunoglobulin (IVIG) therapy.

A small number of cases present as a therapeutic challenge. Often these have been on traditional modes of therapy, and have either failed to respond or have had adverse reactions to these forms of therapy. Switching the type of glucocorticoid therapy may obtain a response. If this fails, trying aggressive glucocorticoid shock intravenous therapy can also be of value. This is often combined with a different immunosuppressive or alternative therapy as listed above.

References:

1. Diseases of the Epidermis. In: Skin Diseases of the Dog and Cat, 2nd edition (2005), Gross, Ihrke, Walder and Affolter pp. 32-35. Link

2. Rosenkrantz WS. Pemphigus: current therapy. Vet Dermatol. 2004 Apr;15(2):90-8. Link

multinucleated cells. The mitotic index ranged from 0 to 45 mitotic figures/10 HPF. Of the 13 cases with adequate follow-up information, four showed local recurrence while three reported metastasis. Eight cats had died at the time of the survey. Survival time post-diagnosis ranged from 0.5 to 36 months. Two cases had metastasized to the submandibular lymph nodes and in a third case, an abdominal mass was detected.
Feline conjunctival melanoma is most frequently found on the bulbar conjunctiva, are mostly round cells and suggest that conjunctival melanoma in cats has a poorer long term prognosis than the same neoplasm in dogs.

3. B. C. McGorum, 2. R. S. Pirie. Antimicrobial associated diarrhoea in the horse. Part 1: Overview, pathogenesis and risk factors. Eq Vet Edu. Volume 21, Issue 11, pages 610-616. link

Antimicrobial associated diarrhoea (AAD) is the most commonly recognised adverse effect of antimicrobial treatment in horses, although its incidence is probably low given the frequency of antimicrobial administration. Clinical signs vary from transient self-limiting diarrhoea to rapidly fatal toxic enterocolitis. AAD prolongs the duration of hospitalisation, increases diagnostic and therapeutic costs, and was associated with a lower case survival rate than other types of acute diarrhoea in one study. Virtually all antimicrobials have been implicated in AAD, but some pose a greater risk than others.

Also in the same series: B. C. McGorum, R. S. Pirie.Antimicrobial associated diarrhoea in the horse. Part 2: Which antimicrobials are associated with AAD in the horse? Eq Vet Edu. Volume 22, Issue 1, pages 43-50.

SIDE STORY

Charity Ride for Prostate Cancer

The Prostate Cancer Charity TourRide South West 05.09.10

Richard and Malcolm are participating in Tour of Britain Pro Ride 2010. This ride is raising money for The Prostate Cancer Charity.

"Stage 4 of the Tour of Britain from Minehead to Teignmouth at 175km is a long day in the saddle for pro's and a testing course for a Tour Ride sportive on Sunday 5th September."

Prostate cancer is the most common cancer in men in the UK. The Charity is fighting prostate cancer on every front through research, information, support and campaigning. Every penny we raise will really make a difference to the lives of men with prostate cancer and their families.

You can help support us by sponsoring us using your credit or debit card. Click onto our secure website using the link below:

http://www.prostatecancercharity. org.uk/Foxyrider

For more information please visit http://www.tourride.co.uk.

LATEST NEWS

Researchers Use Pyrosequencing To Study Canine Intestinal Bacteria

A dog's indiscriminate taste is not always a positive trait. In fact, it often leads to gastrointestinal infections and consequent ailments such as diarrhea and vomiting that come from eating spoiled food. Others develop gastrointestinal diseases such as inflammatory bowel diseases that are not directly attributed to the diet, but are influenced by intestinal bacteria.Researchers at the University of Illinois are making strides in devising dietary interventions to combat these infections through advanced DNA pyrosequencing technology. This new method of DNA sequencing has helped researchers uncover the phylogeny or "who's there" in a healthy dog's gut. Their goal was to obtain a standard that could be used as a comparison to diseased states in the future.

For more information:Medial New Today Article

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