Abbey Veterinary Services
RAPID DIAGNOSTIC HISTOPATHOLOGY & CYTOLOGY

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CASE OF INTEREST

A Case of Hepatocutaneous Syndrome (Necrolytic migratory erythema) in a crossbred dog

By: Richard Fox, Veterinary Pathologist.

A 12 year-old, spayed female crossbred dog presented to a referral practitioner for a six week history of severe self trauma and licking of all four feet. Clinically there was erosion of the digital skin with erythema and severe hyperkeratosis of all digital pads (Figure 1). The dog was lethargic, anorexic and oligodipsic. On blood biochemistry, liver enzymes were elevated (alkaline phosphatase 1500 IU/l, alanine aminotransferase 563 IU/l) but blood glucose was within normal parameters. Ultrasound examination of the liver revealed multiple, diffuse nodules throughout the liver, as well as distended hepatic vasculature. Following biopsy of the digits, further erosive lesions developed in areas of the lips. The dog deteriorated rapidly and the dog was subsequently euthanised on humane grounds.

Histologically (Figure 2) in all sections of skin there was marked diffuse compact parakeratosis, marked oedema of the stratum spinosum/granulosum and the basal and supra-basal keratinocytes were moderately, diffusely, hyperplastic (French flag appearance).

Figure 1. Digital erosion of haired skin and erythema with severe hyperkeratosis (involving all digital pads) (click to enlarge)
(Photos courtesy of Erik J Tjalsma)

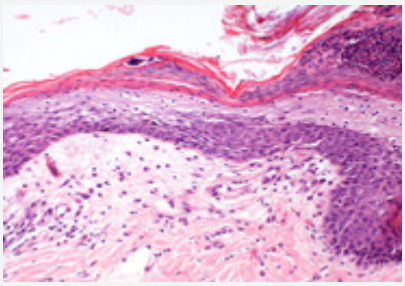

Figure 2. Haired skin with marked diffuse compact parakeratosis, marked oedema of the stratum spinosum/granulosum and basal and supra-basal keratinocyte hyperplasia (French flag appearance) (click to enlarge)
(Photos courtesy of Erik J Tjalsma)

A post-mortem examination was requested and pathological alterations were confined to the liver (Figure 3) which was of reduced size with multinodular and pitted surfaces. Nodules varied from 2mm to 40mm and on cutting of the liver were present throughout the parenchyma and involved all lobes. Histologically (click here for histological image) sections of liver tissue revealed marked disruption of lobular architecture. There were multiple, variably sized nodular organisations of swollen hepatocytes which displayed sinusoidal arrangement but were lacking normal portal triads. Within the connective tissue in areas of parenchymal collapse, multiple small bile ducts, swollen hepatocytes displaying cytoplasmic vacuolation as well as prominent multiple veins and arteries were present.

Figure 3. Liver with multinodular and pitted surfaces with parenchymal nodules varying from 2mm to 40mm involving all lobes. (click to enlarge)

Necrolytic migratory erythema (NME) is a skin eruption first reported in humans with alpha cell pancreatic tumours and elevated plasma glucagon concentrations (i.e., glucagonoma syndrome). A small number of humans with NME do not have a glucagon-secreting tumour

In this issue:

JOURNAL REVIEWS (with e-links)

1.Massive hepatocellular carcinoma in dogs: 48 cases (1992-2002). JLiptak JM, Dernell WS, Monnet E, Powers BE, Bachand AM, Kenney JG, Withrow SJ. J Am Vet Med Assoc. 2004 Oct 15;225(8):1225-30.link

42 dogs were treated surgically, and 6 were managed conservatively. In the surgery group, intra-operative mortality rate was 4.8% with no local recurrence, metastatic rate was 4.8%, and median survival time was > 1,460 days. High alanine aminotransferase and aspartate aminotransferase activities were associated with poor prognosis. Median survival time for the nonsurgery group was 270 days (range, 0 to 415 days), which was significantly less than that of surgically treated dogs. Liver lobectomy is recommended for dogs with massive HCC because tumour-related mortality rate was 15.4 times higher in dogs in the nonsurgery group, compared with the surgery group. Tumour control was excellent after surgical resection with no local recurrence and a low metastatic rate. Prognostic factors were identified, but their clinical relevance was uncertain because only 9.5% of dogs in the surgery group died as a result of their disease.

2. Renal biopsy: a retrospective study of methods and complications in 283 dogs and 65 cats. Vaden SL, Levine JF, Lees GE, Groman RP, Grauer GF, Forrester SD. J Vet Intern Med. 2005 Nov-Dec;19(6):794-801. Link

Renal biopsy is often required to establish a definitive diagnosis in dogs and cats with renal disease. In this retrospective study, we determined the complications of renal biopsy as well as factors that may be associated with development of complications and procurement of adequate renal biopsy specimens in 283 dogs and 65 cats. Data extracted from medical records at 4 institutions were evaluated using logistic regression. Proteinuria was the most common indication for renal biopsy in dogs. Complications were reported in 13.4 and 18.5% of dogs and cats, respectively. The most common complication was severe hemorrhage; hydronephrosis and death were uncomamon. Dogs that developed complications after renal biopsy were more likely to have been 4 to < 7 years of age and > 9 years, to weigh < or = 5 kg, and to have serum creatinine concentrations > 5 mg/dL. The majority of biopsies from both dogs (87.6%) and cats (86.2%) were considered to be of satisfactory quality. Biopsies from dogs were more likely to be of high quality if they were obtained when the patient was under general anesthesia and more likely to contain only renal cortex if they were obtained by surgery. We concluded that renal biopsy is a relatively safe procedure, with a low frequency of severe complications. Hospital practices and patient variables have the potential to impact both the quality of the specimen obtained and the rate of complications.

3. Assessment and management of proteinuria in dogs and cats: 2004 ACVIM Forum Consensus Statement (small animal). Lees GE, Brown SA, Elliott J, Grauer GE, Vaden SL. J Vet Intern Med. 2005 May-Jun;19(3):377-85. Link

[1]. In the veterinary literature, superficial necrolytic dermatitis (SND) (metabolic epidermal necrosis (MEN)) is an uncommon necrotising skin disorder of dogs (and rarely cats [1]) associated with incompletely characterised hepatic disease. .The vast majority of dogs do not have a demonstrable glucagonoma and instead have a hepatopathy with characteristic histopathological and ultrasonographic features (i.e., hepatocutaneous syndrome). Although the exact pathophysiological mechanisms are not known, hypoaminoacidaemia appears to be a consistent finding, suggesting there is underlying cutaneous nutritional deprivation [2].

Histopathological findings are usually consistent but the classical 'French flag' (see above) appearance is not always identified from skin biopsies especially when lesions are relatively chronic. Dogs usually have erosive and ulcerative lesions, with exudation, alopecia and crusting surrounding the pawpads and around the mucocutaneous junctions of the lips, eyes, clawbeds and anus [4].Other lesions can arise at other sites usually involving pressure points. Biopsy sites should include erythematous plaques with mild to moderate adherent crusts avoiding areas of ulceration.

Histological findings from liver tissue consist of severe hydropic and ballooning degeneration. Areas of severe parenchymal collapse result in consolidation of the reticulin fibre network. Foci of nodular hepatocyte regeneration are prominent which can be confused with hepatic cirrhosis. Long term survival of canine patients is limited and treatment is usually palliative [3]. The cause of the degenerative hepatopathy is not known.

References:

1. Kimmel SE, Christiansen W, Byrne KP. Clinicopathological, ultrasonographic, and histopathological findings of superficial necrolytic dermatitis with hepatopathy in a cat. J Am Anim Hosp Assoc. 2003 Jan-Feb;39(1):23-7.
2. Outerbridge CA, Marks SL, Rogers QR. Plasma amino acid concentrations in 36 dogs with histologically confirmed superficial necrolytic dermatitis. Vet Dermatol. 2002 Aug;13(4):177-86.
3. Hill PB, Auxilia ST, Munro E, Genovese L, Silkstone MA, Kirby B. Resolution of skin lesions and long-term survival in a dog with superficial necrolytic dermatitis and liver cirrhosis. J Small Anim Pract. 2000 Nov;41(11):519-23.
4. Thelma Lee Gross *et al*. Skin diseases of the dog and cat : clinical and histopathologic diagnosis. Necrolytic diseases of the skin. 2nd Ed. Oxford. Blackwell Science, 2005. P 75-104.

Emerging data indicate that more attention should be given to the detection, evaluation, monitoring, and treatment of dogs and cats with proteinuria. The purposes of this consensus statement are to describe an appropriate approach for accomplishing these tasks and to provide specific recommendations for assessing and managing dogs and cats with proteinuria based on data that are currently available. Because proteinuria and albuminuria have numerous possible causes, they must be assessed appropriately to determine their implications for the patient. This assessment involves localization of the origin of the proteinuria as well as determination of its persistence and magnitude. Because persistent renal proteinuria usually indicates presence of chronic kidney disease, which sometimes is a progressive disorder, its detection identifies dogs and cats that have increased risk for adverse health outcomes. Thus, urine testing that will detect proteinuria should be a component of the clinical evaluations of dogs and cats under all circumstances that prompt their veterinarians to also perform comprehensive hematologic and serum biochemical evaluations. At a minimum, this testing should consist of a complete urinalysis that includes a satisfactorily accurate semiquantitative test for protein, and positive reactions should be properly followed with further testing. The appropriate response to persistent renal proteinuria depends on the magnitude of proteinuria and the status of the patient. The recommended response generally involves continued monitoring, further investigation, and therapeutic intervention, which should be implemented as an escalating series of inclusive, stepwise responses.

LATEST NEWS

Neuromuscular Disease
For many years we have been carrying out examination on muscle and nerve biopsies using the standard techniques of formalin fixation, paraffin embedding, sectioning and predominantly HE staining. There are very rare occasions when it may be necessary for example to investigate the relative proportions of the different types of muscle fibre. This can only be done on frozen tissue with frozen sections using special histochemical staining.

The Royal (Dick) School of Veterinary Studies at the University of Edinburgh has set up a Neuromuscular Disease Laboratory and they are able to carry out these specialist techniques on the rare occasion when these are required. If you are unsure whether straightforward HE sections would be suitable for a diagnosis of your particular case then please give us a ring to discuss the case and we can advise on which technique would be best for a suspected diagnosis.

SIDE STORY

Gallery
Our gallery section includes several more cytology images. We anticipate this to increase gradually over time depending on when suitable cases become apparent. If you wish to see specific examples shown on the site please let us know. We would be more than happy to find previous cases or cases you have submitted if they are suitable.

If you wish to subscribe/unsubscribe to the e-newsletter please submit your e-mail address on any page our our new website!

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BIOPSY TIPS - DIATHERMY

When using electrical or thermal cautery to remove tissue for histological examination the biopsy size is crucial. Tissue under 10 mm in diameter will have undergone extensive coagulation artefact which makes interpretation very difficult to impossible. If the tissue biopsy is small use a core punch biopsy or a surgical blade and then cauterise the site afterwards for haemostasis.

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