



The Cutting Edge

Halifax Veterinary Centre Referral Services

205 Bridge Street
Nelson
Ph: 03 5483871
Fax: 03 5481712
Email: info@halifaxvet.co.nz

CASE REPORT

Nephrotic Syndrome in a Cat

by Chris Welland

Sirius, a 6-year-old, neutered male presented for marked weight loss and an acute onset of polydipsia. The physical exam was unremarkable except for mild dehydration (5% approx).

Urinalysis revealed: specific gravity 1.017; glucose, bilirubin, ketones, blood and urobilinogen were all negative on the dip stick. pH 6.5, protein 3+.

The urine cytology was unremarkable.

Blood results (SpotChem analyser)

Urea 37.7 mmol/L

Glucose 5.5 mmol/L

ALP 21 IU/L

ALT 13 IU/L

Creatinine 343 μ mol/L

Cholesterol 10.34 mmol/L

Calcium 2.7 mmol/L

Albumin 17 g/L

Blood pressure 194 mm Hg 3cm cuff. Protein creatinine ratio = 7.85.

Diagnosis

Nephrotic syndrome with secondary renal failure.

Discussion

Nephrotic syndrome (NS) is appropriately defined as concurrent proteinuria, hypoproteinemia, hypercholesterolemia, and oedema or ascites. Sirius met these requirements except for the lack of ascites

and oedema (probably because his albumin was still > 15g/dL).

Common complications of nephrotic syndrome are hypertension, thromboembolic disease (due to the loss of Antithrombin III) and secondary renal failure with the development of CRF. Sirius had developed hypertension 10.5

Treatment

Treat the underlying cause where possible — proteinuria may resolve. Options for treatment are much more limited and the prognosis becomes more guarded once the patient is azotaemic. ACE inhibitors remain the cornerstone of treatment in reducing glomerular protein loss (and secondary tubular damage), improving appetite and ultimately increasing survival times in severely proteinuric patients. They can also be used in those patients with concurrent CRF. The most studied drug in cats is benazepril (Fortekor). Thromboprophylaxis - unfortunately we are unable at present to measure ATIII levels in our small animal patients in NZ - could consider the use of low molecular weight heparin, aspirin or clopidogrel.

In markedly hypertensive patients amlodipene may be required in addition to an ACEI.

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Renal diets, omega 3s, potassium supplements and other standard treatments for concurrent CRF may also be required. Immunosuppressives can be effective, but should only be considered normally in nonazotaemic patients. (See below.)

Do we need to biopsy?

Histology can help distinguish between the different forms of glomerulonephritis:

Membranous GN is characterized by a thickened glomerular basement membrane (GBM).

Proliferative (mesangio proliferative) GN is characterized by glomerular hypercellularity with accumulation of mesangial matrix. Membranoproliferative GN is a combination of hypercellularity and increased thickness of the GBM.

Glomerulosclerosis is an increase in matrix and glomerular scarring.

Minimal change disease is characterized by normal to mild increases in mesangial cell proliferation, abnormalities of podocyte foot processes, and a lack of immunoglobulin deposition on immunofluorescence. Electron microscopy is required to confirm the diagnosis (but the lack of other changes could lead to a diagnosis by default with standard histo).

Why is this important? It can lead to a more accurate prognosis and can determine the medication required (which type of immunosuppressives). In humans minimal change disease (rare in cats?) has an excellent prognosis — 90% of people respond to prednisone.

BUT membranous GN is the most common type in cats and Sirius' signalment would fit with this form. MGN is more common in male cats. Mean age is only 3.6 years and due to severe proteinuria many present with NS. Would I biopsy? I would generally only consider biopsy after having ruled out secondary disease and in a non azotaemic patient.

Monitoring

Day to day variations in Urine protein : creatinine ratios (UPC) of up to 50% in dogs and 90% in cats have been described. Ideally averaging 2-4 UPCs over 3-5 days is ideal but seldom done due to costs. Establishing a trend is more important than putting too much weight on individual results.

Drug Profile — Levetiracetam (Keppra®)

Levetiracetam is used in human and veterinary medicine as an anti-seizure medication. The precise mechanism(s) of action is not fully understood. It has been shown to affect intra-neuronal Ca⁺⁺ stores and has a strong binding affinity for the synaptic vesicle protein 2A, which is involved in vesicle fusion/neurotransmitter exocytosis. In animal models (including the dog) levetiracetam has a dose-dependent inhibitory effect on on "kindling", whilst withdrawal after chronic administration does not decrease the seizure threshold. Levetiracetam has also been shown to have anxiolytic properties and an absence of undesirable effects on cognitive function.

In dogs the oral bioavailability is close to 100% with a half-life of 4 to 6 hours. The pharmacological effects however extend far beyond this half-life. Metabolism is predominantly by enzymatic hydrolysis, which is independent of the hepatic cytochrome P-450 system. Excretion occurs via the renal system. This drug appears extremely well tolerated with a very wide safety margin with no known drug-drug interactions. Formal studies in dogs are currently being performed. An initial study in dogs using the

injectable formulation revealed excellent results in treating status epilepticus.

Experience with levetiracetam by specialist veterinary neurologists in USA and Europe have indicated significant benefit in treating dogs (and a smaller number of cats) with severe difficult to control seizures when used alongside phenobarbitone or as the sole treatment. The recommended starting dose is 10 mg/kg q 8-12 hrs with an estimated dose range of 5 to 25 mg/kg.

Levetiracetam is available in NZ under the trade name Keppra®. Unfortunately no generic formulations are currently available - making this drug expensive to use. Keppra® comes as a 250 mg, 500mg and 1000mg film-coated tablets or a 100mg/ml oral suspension. Splitting the 1000mg tablets is the most cost-effective dosing option but still costs approximately \$6.00 per day for a 20-kg dog. We have experience with one dog so far who has had very difficult to control idiopathic epilepsy who was being treated with high dose of both phenobarbitone and potassium bromide - we have seen an excellent reduction in seizure frequency and are currently weaning the dog off phenobarbitone. The potassium bromide has been discontinued altogether.

What's Your Diagnosis?

History

A 9-year-old castrated male Golden Retriever was presented for a newly identified skin mass on the right front paw. The owner was uncertain how long the lump had been present but had noted the dog licking excessively at the paw over the previous 24 hours. The dog had remained bright and alert with a normal appetite. There was no associated lameness.

Physical Examination

A five to seven millimetre cutaneous mass was identified medially adjacent to the nail bed of digit II. The lesion was hairless, raised, had fissures on the surface and was mildly painful when palpated. The draining right prescapular lymph node was normal in size. (See photo 1 for appearance).

A fine-needle aspirate was performed for cytological analysis — the results of which can be seen in Photos 2, 3 and 4.

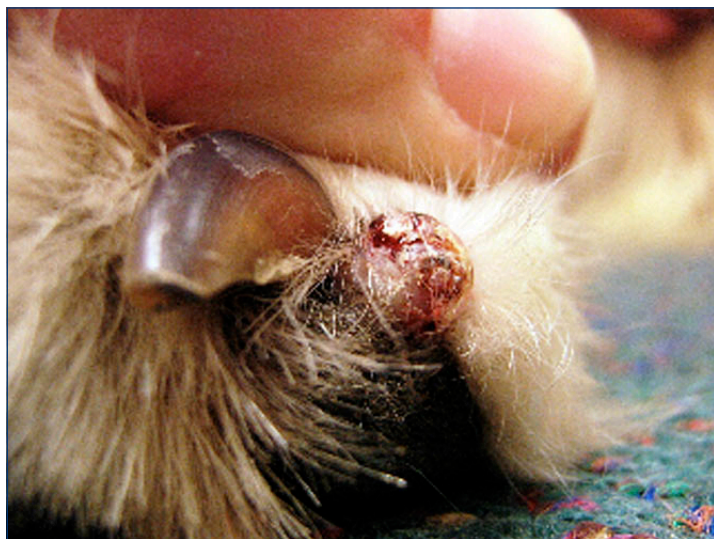


Photo 1. Physical appearance of skin lesion

Question 1

Based on the history and physical examination what differential diagnoses would you consider?

Question 2

Describe the cytological appearance of the cells in Photos 2, 3 and 4 and give your diagnosis.

Photo 2. Cytological appearance of cells (10x magnification)

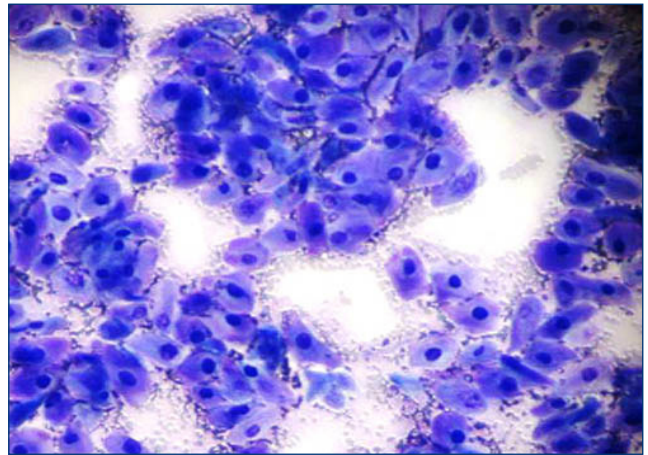


Photo 3. High power magnification (40x)

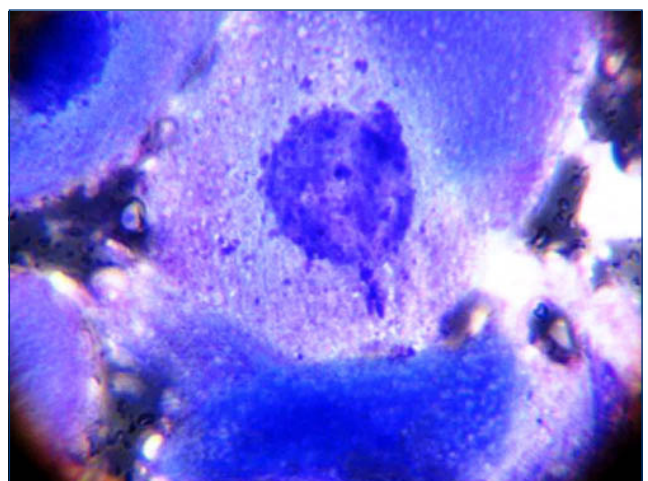
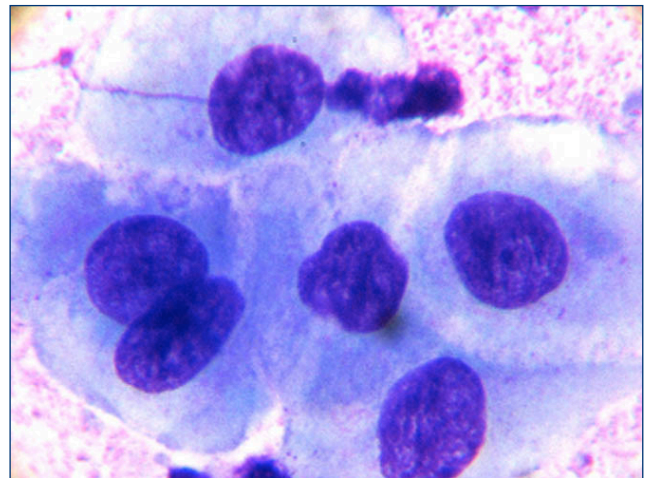


Photo 4. High power magnification (100x)



What's Your Diagnosis? – Answers

1. DDx: Squamous cell carcinoma, Melanoma, Papilloma, Keratoacanthoma, Inflammatory/ Infectious granuloma.

2. There is a population of epithelial cells amongst a background of red blood cells. The epithelial cells are variable in appearance with some anuclear squames present alongside a variable nuclear/cytoplasmic maturation. The cytoplasm stains from aqua blue to a deep basophilic colour. The nucleus stains a deep blue-purple and at higher power there is evidence of a stippled chromatin pattern with some binucleate cells.

This cytological appearance is most consistent with Squamous Cell Carcinoma.

Discussion

Subungual tumours (SUT) are common in dogs and account for

about 12% of subungual lesions. One third of SUT are squamous cell carcinomas (SCC) with melanoma, mesenchymal and mast cell tumours the next most common in decreasing order. SUT in cats are rare and are usually metastatic lesions from pulmonary masses (adenocarcinoma and SCC). Many SUT are locally invasive causing osteolytic destruction of P3 — therefore radiography should always be included in the diagnostic work up of subungual lesions.

Subungual SCC is a locally invasive tumour often resulting in P3 lysis. It occurs in older dogs with a mean age of nine years. Seventy five percent of affected dogs are large breed and of these 66% of cases occur in dogs with a black coat (Labradors and standard Poodles being the most commonly affected breeds). The lesions are usually solitary in nature

with a raised hairless appearance and often become ulcerated with secondary bacterial infection. SCC in this site has a very low metastatic potential with one and two-year survival times reported to be approximately 76% and 43%, respectively. Local recurrence is more likely if the initial surgical management was conservative — it is therefore recommended that amputation at the level metacarpal/metatarsal-phalangeal joint be performed.

A syndrome of multiple digital SCC in the dog has been reported as well as a Rottweiler in NZ who presented on four separate occasions with tumours on four separate toes. Three different tumours were identified: two x SCC, one melanocytoma and one keratoacanthoma (intracutaneous cornifying epithelioma).

WEB RESOURCES

<http://veterinarymedicine.dvm360.com>

This is an excellent website with hundreds of useful articles and videos for both veterinarians and vet nurses. There are also some useful business management articles and plenty of links to other useful sites.