



REFERRAL NEWS

AUTUMN 2017

In this edition:

Lymphoma in the Dog: A Current Perspective

Clinical Work at Rosemary Lodge

Next CPD date

- Wednesday 18th October 2017

- Oncology: Medical and Surgical Aspects

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Lymphoma in the Dog: A Current Perspective

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Lymphoma in the dog is the most common hematopoietic malignancy we expect to deal with in veterinary practice. Estimated to occur in 24/100,000 dogs in the general population at risk, Golden Retrievers, German Shepherd Dogs, Collies, Standard Poodles, Old English Sheep Dogs and Scottish Terriers are over represented. Veterinarians may well be faced with the challenge of diagnosis, prognosis and recommendations for treatment fairly frequently. The decision to refer the patient will be based both upon knowledge of the disease and presentation to the owner. With clinical application and availability of diagnostics developed over the past 30 years we can fairly well predict biologic behaviour in most instances and recommend appropriate treatment. Lymphoma is quite responsive to chemotherapy and good quality of life may often be achieved for a year or more. Unfortunately, in the majority of cases we will not provide for cure and long-term response may be seen in only 20 percent of dogs treated.

Diagnosis and Classification:

The most common presentation in the dog is generalised lymphadenopathy developing over a few short weeks. The patient may be unaffected or have nonspecific illness. Regardless the time to progression without treatment is usually only an additional three weeks. Diagnosis may be achieved rapidly by performing fine needle aspiration of a lymph node submitted for cytology with follow up testing for immunophenotype for determination of T or B cell lineage. The majority of dogs will have an intermediate or high grade lymphoma and the determination of a T cell immunophenotype is associated with a poorer prognosis compared to those with the more common B cell immunophenotype. Clonality, the determination of single cell line proliferation of either T or B cells as seen in lymphoma versus multiple mixed cell line proliferation in responsive lymphoid hyperplasia may be established by polymerase chain reaction for DNA sequences using specific primers which have been developed for the dog. This test, PARR (PCR for Antigen Receptor Rearrangement)

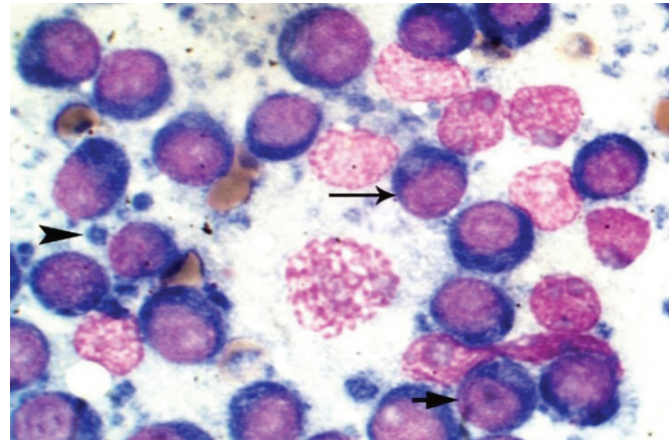
Autumn update from BVR...

Welcome to our latest newsletter. The lead article on lymphoma from Bob Matus will be of interest to all small animal practitioners, and is a taster of our upcoming CPD day on Medical and Surgical Aspects of Oncology. We hope as many of you as possible will be able to join us for this (feedback from delegates is consistently high).

We remain as busy as ever here at Rosemary Lodge. We have recently welcomed Ted Corfield as Assistant Referral Surgeon, and you will meet him on our CPD day.

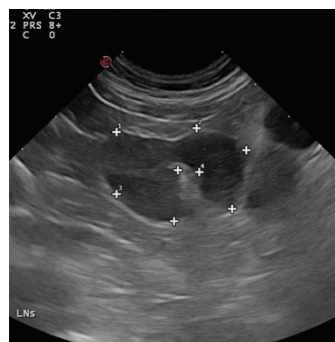
Once again we have the builders in at the hospital. The cat ward is moving to a new part of the building and will be upgraded to full ISFM standards. We are also creating two new consulting rooms which will allow us to offer more referral appointments to your clients.

Lymphoma in the Dog: A Current Perspective continued.

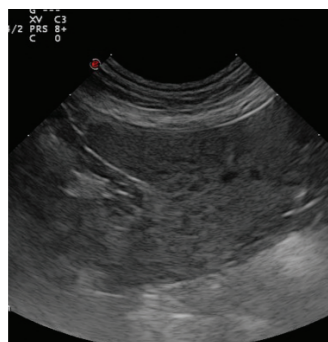


Cytology: large cell canine lymphoma preparation (from Vet Res Forum published online Mar 2016 unrestricted access) from a dog with B cell lymphoma.

may be performed from lymph node aspirates on stained or unstained slides. Still however tissue biopsy does establish further basis on which to identify lymphoma versus lymphoid hyperplasia and is necessary to classify lower grade versus the more common higher grade lymphoma. Immunophenotype may then be confirmed by immunohistochemical staining. On referral evaluation, we may well recommend a minimally invasive Tru Cut biopsy procedure to obtain a tissue specimen if the diagnosis has been established by cytology alone. In those patients that present with evidence of leukaemia flow cytometry may be recommended. This test involves passing a single cell suspension through a gated laser light source to establish groups of cells by size, physical characteristics and immunofluorescence utilizing monoclonal antibodies to determine cell surface protein groups associated with cellular differentiation. It may be performed on lymph node aspirates and peripheral blood or bone marrow samples to establish a more definitive diagnosis of Stage V lymphoma versus primary high grade lymphoid leukaemia which has a poorer prognosis or low grade lymphoid leukaemia which might have a better prognosis.



Ultrasound image abdominal lymph nodes from a dog with large cell lymphoma; note outlined mesenteric nodes.



Ultrasound image spleen from a dog with large cell lymphoma; note mottled echogenic appearance of parenchyma suggesting infiltrative process.

Biomarkers in Diagnosis and Follow Up

There are now blood tests available that may provide information in the diagnosis and management of lymphoma. C reactive protein and haptoglobin are

produced by the liver in response to inflammation and high levels are known to occur in dogs with lymphoma. Although not diagnostic for lymphoma in and of themselves, they may be of value in combination with cytopathology in establishing diagnosis and relapse in follow up of treatment response. What we do not know however is whether early recognition of possible relapse identified only by the presence of elevation in these proteins without recurrence of clinical signs and changes in physical exam or routine laboratory testing will allow us to routinely recommend initiation of treatment at that time.

Clinical Stage and Treatment

In establishing clinical stage of disease in lymphoma there is the general consensus that dogs with Stage I and II disease (the presence of only regional nodal involvement) may have a more prolonged remission compared to dogs with the more commonly presenting stage III (generalised lymphadenopathy) disease but there is controversy on whether or not more advanced disease Stage IV (liver and spleen involvement) is truly predictive. This may be due to past studies utilizing only radiography for determination of stage versus ultrasound imaging and fine needle aspiration which may be more commonly performed today. Stage V lymphoma (peripheral blood and bone marrow involvement) must be differentiated from aggressive acute lymphoblastic lymphoid leukaemia or the more indolent lower grade chronic lymphocytic leukaemia all of which carry a different prognosis. Flow cytometry of peripheral blood and/or lymph node aspirates is the most sensitive diagnostic test for this determination by which again cell size, immunophenotype and other markers of cellular differentiation may be established.

In general treatment may be considered with a minimal data base of routine laboratory testing (CBC, biochemistry profile) and lymph node cytology and immunophenotype. Prognosis for the otherwise healthy dog with generalised stage III-V lymphoma is similar based upon published studies. However notable observed changes in physical status such as major organomegaly on exam, marked lymphocytosis, anaemia, and hypercalcaemia on laboratory studies may affect prognosis. A major prognostic indicator of stage of disease is whether or not the dog is showing signs of clinical illness (substage B) or not (substage A). In all studies to date physical condition as a sub-stage significantly affects response and survival. In the severely compromised patient we will attempt to stabilize with appropriate supportive care either as an outpatient or in hospital prior to administration of induction chemotherapy.

Chemotherapy Protocols:

Treatment for dogs with lymphoma is generally chemotherapy for which several protocols have been established and are recommended based upon the individual patient characteristics. We have evolved from the basic COP [cyclophosphamide, vincristine (Oncovin), prednisone] to CHOP [COP plus doxorubicin (hydroxydaunorubicin)] as standard protocols for dogs with high grade lymphoma. However, it is reasonable

to consider an alkylating agent based protocol such as LOPP (lomustine, vincristine, procarbazine, prednisone) in dogs with high grade T cell lymphoma. The alkylating based protocols are more intensive in our attempts to better control the progression of T cell lymphoma. They are commonly used to treat relapse of lymphoma in combination with L-asparaginase but it is still unclear whether or not they are truly more effective than using CHOP based protocols for initial chemotherapy. We have also modified the length of treatment protocols and largely abandoned maintenance phase treatment altogether. Most recently the use of a short 16 week CHOP type protocol has shown equivalent results to the standard six month length of treatment. Repeated treatment at time of relapse may be of equal value to the more prolonged protocols in dogs with higher grade lymphoma. Treatment of lower grade lymphoma of either B or T cell phenotype is usually less intensive and response may be achieved with single agent chlorambucil and prednisone. In some cases of "indolent" B cell or low grade T cell lymphoma we may not initiate treatment until progression of disease is observed which may be many months to occurrence.

Other more novel approaches to treatment have been available in the USA for the past few years with conditional approval of monoclonal antibodies for B cell and T cell lymphoma (Anti CD20, Aratana; Anti CD52, Novartis). However, they failed to demonstrate overall significant clinical improvement benefit and have now been withdrawn by the manufacturers. A commercial lymphoma DNA vaccine (Oncept, Merial) is available with conditional approval but again is of questionable value in improving treatment outcome. A new conditionally approved chemotherapy drug, rabacfosadine (Tanovea, Vet-DC) is receiving great interest by veterinary oncologists in the USA as well. This drug is a dual acting pro analogue of guanine which inhibits DNA synthesis and preferentially accumulates in canine lymphoid cells. Tanovea has demonstrated clinically effective response as a single agent and in combination with doxorubicin in dogs with both naive and relapsed lymphoma. These two products however are not currently available in the UK.

Summary:

Following the diagnosis of lymphoma, the biggest challenge may be to provide help to the owner in deciding on referral for further diagnostic evaluation and treatment. As lymphoma is not curable the questions are most often related to benefit and duress of diagnostic testing and treatment, practicality of doing so and costs involved. General surveys to assess these questions are of limited availability but at least in the USA for the most part, owners of dogs with lymphoma are appreciative of the attempt to provide good life for a period of time. Diagnostic and treatment plans may be modified to accommodate individual circumstances without sacrificing professional integrity or the best interests of the patient and owner. Following the decision to treat based upon owner personal opinion of benefit and life preferences cost

is often the next major consideration, which in the UK is affected by insurance, unlike in the USA where most owners do not insure their pet's healthcare needs. We may well be able offer treatment protocol alternatives for the owner to consider in this regard should the need be present. Again, considering the response of lymphoma to a varied number of protocols there are reasonable approaches for interchanging drugs and timing/duration of planned treatment. Our goals are to provide for professional expertise and high quality patient care in all cancer patient referrals to establish diagnosis, prognosis and treatment.

CPD by Bath Veterinary Referrals

Our next low cost CPD course is titled:

Oncology: Medical and Surgical Aspects

Wednesday 18th October 2017

9.30am-4.30pm

Coombe Lodge, Blagdon, BS40 7RE

Course Fee - £110 per delegate

LECTURES WILL INCLUDE:

- Tumours of the urogenital tract
- Canine Lymphoma
- Oral Neoplasia
- Canine Mast Cell Tumour, current perspective and chemotherapy

ZERO Referral Consultation FEES for any UK forces staff



supporting British Armed Forces



Cases recently seen

Methylmalonic aciduria in a 10 month old Shih Tzu, trigeminal nerve sheath tumour with intracranial invasion, grass seed foreign body in lungs requiring lung lobectomy, ventricular septal defect in a kitten, splenic haemangiosarcoma with hepatic and intracranial metastasis, a seven year old DSH with lower grade abdominal mesenteric nodal lymphoma and a leukemoid response resembling myelomonocytic leukaemia; a six year old Bernese Mountain dog with transitional cell carcinoma of the urinary bladder and intraluminal blood clot causing urethral obstruction with an associated syndrome of DIC and clinical thrombocytopenia.

Types of referral seen

- Internal medicine
- Soft tissue surgery
- Endoscopy/laparoscopy
- Medical and surgical oncology
- Ophthalmology
- Neurology
- Cardiology
- Orthopaedic and fracture repair
- Onsite MRI/CT scanning
- Hydro/physiotherapy

Why choose Bath Veterinary Referrals?

- We pride ourselves on giving you the highest level of service
- We strive to enhance your reputation, looking after your clients and their pets in a way you would be proud of
- We offer a caring, friendly and personalised service. We keep clients and referring vets informed at all times
- We have a superb team of night nurses and night vets, a flagship hospital and the very latest equipment

Organising a referral is simple

Just phone Rosemary Lodge Veterinary Hospital on **01225 832521** and book in with one of our receptionists.

One of our clinicians will be very happy to discuss the case details prior to arranging the referral. Once you have made contact we will normally ask to speak directly to the pet's owner to swiftly arrange an appointment that fits in to their timetable. We do ask you email, fax or post us any relevant history with a supporting referral letter.

We will always do our best to fit in any emergency cases immediately and see them on the day you call us.

Now Available: Free Film Reading

Post your X-Rays to Rosemary Lodge or email them to contact@bathvetreferrals.co.uk to receive a free verbal report from one of our clinicians



Our clinicians

Alex Gough MA VetMB CertSAM CertVC PGCert (Neuroimaging) MRCVS - Head of Internal Medicine

Alasdair Hotston Moore MA VetMB CertSAC CertVR CertSAS CertMed MRCVS - Head of Surgery

Jon Shippam BVSc CertSAS MRCVS - Orthopaedic Surgeon

Jenny Lambert BVM&S CertVOphthal MRCVS - Ophthalmology

Lisa Gardbaum BVetMed CertSAM MRCVS - Internal Medicine

Robert E Matus DVM MS Diplomate ACVIM (Oncology and SAIM) MRCVS - Oncology and Internal Medicine

Samantha Lane BVSc PGCertSAS MRCVS - Surgeon

Federica Manna DVM MRCVS - Assistant to Internal Medicine

J. Andrew Jagoe MVB PhD CertSAM MRCVS - Internal Medicine

Ted Corfield BVSc MRCVS - Assistant Referral Surgeon