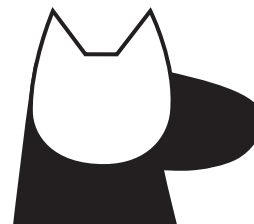


WEAR REFERRALS NEWSLETTER

August 2006



NEWS:

We are pleased to announce the expansion of our services with some exciting new developments; An in-house MRI scanner, great CPD and some post-operative rehabilitation news.

MAGNETIC RESONANCE SCANNER:

Firstly, we are proud to be able to inform you that our permanently on-site magnetic resonance (MR) scanner should be fully available for clinical cases by the middle of August. This means that the MR scanner it will be available 24/7, 365 days a year. It enables us to scan urgent cases the same day or the next day (including weekends). In the meantime, staff at Wear Referrals are undergoing extensive training to educate themselves in the technical and clinical aspects of MRI. The MR scanner will able us to offer referring practices an advanced imaging service, with a minimal delay for your clients' animals. As part of the MR scanner launch we will organise an evening meeting for referring veterinary surgeons later in October to explain and inform them on the great imaging modalities and the indications of magnetic resonance imaging (a further mailing will follow).

CPD:

After the successful evening meetings on hip dysplasia and anaesthesia we would like to inform you about our next CPD meeting. This great value for money meeting will be on the 20th of September (see enclosed information). The subject will be neurology for the general practitioner and the speaker will be Simon Platt, who is the senior neurologist at the Animal Health Trust and, as most of you know, is an internationally recognised veterinary neurologist.

STAFF:

As part of our professional after-care and rehabilitation program for our orthopaedic and spinal patients, we now work in close conjunction with a fully qualified veterinary physiotherapist (Rebecca Heald) and a sports-physiotherapist from the human field (Ivan Whitfield). This will maximise final outcome and reduce total rehabilitation time for our patients. Where necessary Rebecca and Ivan will treat

patients (especially spinal patients, severe trauma) on site at Wear Referrals.

Ivan Whitfield (MHFST) is a Sports Therapist specialising in the management and rehabilitation of musculoskeletal conditions. Over the last five years he has had the good fortune to work with many elite and professional athletes, specifically Team GB cyclists and, with regard to rugby union, players representing Newcastle Falcons and England RFUW international squad members. His involvement in all things non-human began when, ten years ago, he developed an interest in racing Siberian Huskies, a sport that requires knowledge of canine anatomy, physiology, performance and nutrition. He quickly realised through his own experiences that rehabilitating animals was only a step away from his usual patients and over the last three years has undertaken additional training in equine and canine disciplines including Veterinary Hydrotherapy. A distinction he likes to make since 'hydrotherapy' has become synonymous with dog swimming over the last few years and it is important to ensure rehabilitation cases are managed professionally. Ivan is currently at the University of Teesside reading for a specialist degree in sports therapy focusing on orthopaedics and trauma.

Rebecca Heald BSc ((Hons) PgDIP (RVC, London), MCSP, ACPAT) has many years of experience with animals, having grown up with dogs and horses and has been a regular competitor in British Show Jumping Association. In order to become a veterinary physiotherapist she first completed a BSc (hons) degree in human physiotherapy at the University of Teesside. She then worked for the NHS for two years, as required before studying for eighteen months at the Royal Veterinary College, London, and gained the post graduate diploma in Veterinary Physiotherapy. She completed her practical training with Amanda Sutton (Olympic Equine Team Physiotherapist) in Winchester.

Page 2 of this newsletter contains an interesting case report. Thanks to all our referring practices for your continuing support.

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CASE REPORT:

CASE HISTORY

A six-year-old neutered male Staffordshire Bull Terrier was presented with a two-month slow progressive history of hind limb weakness, faecal incontinence and difficulties climbing stairs. No mental abnormalities were observed by the owner. General examination showed a generalised ataxia and worn nails on the hind legs. Hypermetria, paresis posterior, a reduced anal reflex, a reduced perineal reflex and clonus on the patellar reflexes were found. These findings were consistent with multi-focal neurological disease. A full blood profile and urine analysis were within normal range. Cisternal myelography, lumbar epidurography and cerebro-spinal fluid analysis were normal. Anti-body tests for Toxoplasma IgM/IgG, Neospora and Distemper virus were negative. MRI scanning of the brain and the spine revealed generalised increased signal on T2-weighted images of the cerebellum. Additional genetic testing for L-2-hydroxyglutaric aciduria (L-2-HGA) showed that both genes were abnormal.

L-2-HGA

In the past few years a small number of Staffordshire Bull Terriers have been diagnosed with an inborn error in metabolism, its clinical name is L-2-hydroxyglutaric aciduria or L-2-HGA. L-2-HGA is a neuro-metabolic disorder characterised by elevated levels of L-2-hydroxyglutaric acid in urine, plasma and cerebrospinal fluid. Dogs from totally different bloodlines have been found to be sufferers and the number of affected dogs diagnosed has risen. Recently L-2-HGA has also been diagnosed in a West Highland White Terrier.

CLINICAL SYMPTOMS

L-2-HGA affects the central nervous system, with clinical signs usually apparent between six months and one year (although they can appear up to eight years). Both male and female dogs are equally affected. Symptoms include epileptic seizures (acute onset, young age), "wobbly" gait, tremors, muscle stiffness as a result of exercise or excitement, exercise intolerance, lethargy, dementia (staring at walls, getting stuck under tables and in corners, loss of obedience and house training), anxiety attacks and altered behaviour.

CLINICAL EXAM

The clinical signs evident in L-2-HGA are not specific for the disease and may be caused by a variety of other diseases, including causes as varied as primary epilepsy, brain tumours, spinal disease and meningitis. Neurological examination can show a hypermetric gait hyper-reflexia of the spinal reflexes and paresis posterior. Routine blood tests, urine analysis and CSF analysis are within normal range. Serology should be routinely run to exclude Toxoplasma, Neospora and Distemper.

DIAGNOSTIC IMAGING

Survey radiography and myelography are normal. Fortunately L-2-HGA has characteristic features on magnetic resonance imaging, which allow it to be differentiated from most other diseases. L-2-HGA is characterised by bilateral diffuse gray matter hyper-intensity on T2-weighted images of the thalamus, hypo-thalamus, dentate nucleus, basal ganglia, dorsal brainstem, cerebellar nuclei and cerebellar gyri. These changes are consistent with a metabolic or toxic insult to the gray matter. The lesions are mildly hypo-intense on T1-weighted images and no contrast

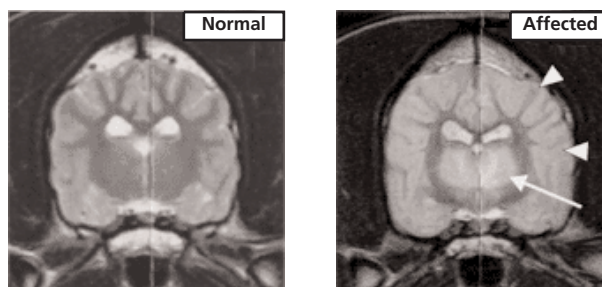


Fig.1: MRI sagittal T2 weighted images of an affected and an unaffected dog

enhancement or mass effect is seen. Many affected dogs are therefore identified based on characteristic MRI features combined with the history and clinical examination.

DIAGNOSIS

Definitive confirmation of L-2-HGA (in cases with the typical MRI appearance and in those cases where MRI is not available) used to be made by demonstrating elevated concentrations of L-2-Hydroxyglutarate by stable-isotope-dilution gas chromatography-mass spectrometry in blood, csf and urine samples. Over the last few years however, a genetic test has been developed to diagnose L-2-HGA.

TREATMENT & PROGNOSIS:

L-2-HGA is slowly progressive and does not respond to medication. Seizures can often be (temporary) controlled with the routinely used anti-epileptic drugs. Reasons for euthanasia are uncontrollable seizures and progressive paresis.

GENETICS

The mutation, or change to the structure of the gene, probably occurred spontaneously in a single dog but once in the population has been inherited from generation to generation like any other gene. This mutation has recently been identified at the Animal Health Trust. The disorder shows (as it is the case in humans) an autosomal recessive mode of inheritance: two copies of the defective gene (one inherited from each parent) have to be present for a dog to be affected by the disease. Individuals with one copy of the defective gene and one copy of the normal gene - called carriers - show no symptoms but can pass the defective gene onto their offspring. When two apparently healthy carriers are crossed, 25% (on average) of the offspring will be affected by the disease, 25% will be clear and the remaining 50% will themselves be carriers

Using the information from this research, a DNA test for the disease has been developed. This test not only diagnoses dogs affected with this disease but can also detect those dogs which are carriers, displaying no symptoms of the disease but able to produce affected pups. Carriers could not be detected by the tests previously available, which involved either a blood or urine test detecting elevated levels of L-2-hydroxyglutarate or magnetic resonance imaging. Under most circumstances, there will be a much greater number of carriers than affected animals in a population. It is important to eliminate such carriers from a breeding population since they represent a hidden reservoir of the disease that can produce affected dogs at any time.

The test (oral swab or EDTA blood) is available now at the AHT and can be used for two purposes; firstly to confirm clinical suspicion and secondly to assist dog breeders in eradication this disease.