WEAR REFERRALS

# MENINGO-ARTERITIS (meningitis) and MENINGO-ENCEPHALO-MYELITIS of Unknown Origin (MUO)

## INTRODUCTION:

Most people have never heard of MUO, meningitis or any other form of central nervous system inflammation until they have a dog with this progressive neurological disease. At Wear Referrals we see patients with MUO or meningitis on an almost daily basis and they are therefore one of the most commonly diagnosed diseases of the central nervous system in dogs. We understand how stressful it can be for owners when they hear that their beloved pet has been diagnosed with MUO or meningitis. This information sheet provides a summary of these conditions in an understandable form.

The general process of inflammation involves the infiltration of normal tissues by cells of the immune system. These cells are like the armed police of the body. They go to the area where they are called and release destructive biochemicals with the goal of obliterating an area of invasion by infectious organisms or of dead or diseased tissues. We do not exactly know why MUO and meningitis occur but they are thought to have an immune-mediated background. It is important to note that both MUO and meningitis are generally not infectious diseases in contrast to meningitis in humans where they tend to be viral or bacterial on origin.

MUO involves infiltration of the central nervous system by cells called "mononuclear cells". These cells normally engulf and destroy debris. These cells form cuffs around the blood vessels of the brain and spinal cord (mostly in the white matter). The cuffs join at adjacent vessels forming actual masses/nodules. MUO can affect all areas of the brain, the spinal cord and the membranes that surround them. In meningitis patients we see predominantly "neutrophilic" cells in the spinal fluid and these cells are located around the meningi. The meningi are the layers of tissue which surround the brain and the spinal cord.

## THE CLINICAL PICTURE OF MUO & MENINGITIS

Both MUO and Meningitis are rapidly progressive diseases which are life threatening if not treated promptly. The classical patient with MUO is a young to middle-aged small breed dog (terrier) of either gender although any dog can be affected. What sort of neurological signs are seen depend on what area of the nervous system is involved. Seizures, neck pain, drunken gait, walking in circles, blindness, listlessness, tilted head, facial abnormalities, problems swallowing and weakness can be seen. This does not leave out much in the way of neurological symptoms.

The main clinical symptoms in dogs with meningitis are neck pain, fever and depression. These patients tend to be mainly young (<2 years) large breed dogs . The Beagle is a smaller breed dog in which meningitis is frequently diagnosed. Some dog can suffer from poly-arthritis (inflamed joints) at the same time as suffering from meningitis (Akita's, Bernese Mountain dog).

## TYPES OF MUO

There are several different of MUO which tend to be breed related. The main types are:

- Granulomatous Meningo-Encephalitis (GME)
- Necrotising Meningo-Encephalomyelitis (NME)
- Necrotising Leuco-Encephalitis (NLE)
- Idiopathic Tremor Syndrome (ITS)

GME can be focal (limited to one location in the nervous system), disseminated or multifocal (involving many locations in the nervous system) and ophthalmic (involving the optic nerve/eye). A patient may have more than one type at the same time. GME is mostly seen in small white fully dogs like the West Highland White Terrier, Shih Tzu and Malteser. The focal type of GME typically can have a slower onset (months) while the disseminated form is more rapid (sometimes days to a few weeks). Obviously, the disseminated form has a larger variety of signs within the same patient. The ophthalmic form most commonly shows up as sudden, generally permanent blindness. It can affect one or both eyes. The disseminated form has a particularly poor prognosis; in one (relatively old) study the median survival time after diagnosis was 8 days, a testament to the rapid progression, seriousness and severity of this condition.

Some of the other types are also relatively breed specific and NME and NLE have been described in Pugs (Pug encephalitis), Maltese, YTs, Chihuahuas, Papillon, Shih Tzu, Coton de Tulear, and Brussels Griffon.

Idiopathic Tremor Syndrome (also called "white shaker syndrome") occurs mainly in small breeds like the Maltese, WHWTs and Cocker Spaniels. Again, it is mostly seen between 1-5 years of age. The classic symptoms are tremors but other signs of central nervous system disease can also be seen.

## MAKING THE DIAGNOSIS

The diagnosis is made based on the patient's history, breed, age, the clinical examination, bloods tests, urine analysis, radiographs, MRI and spinal fluid analysis. Blood panels and urinalysis form the foundation of evaluation and determination of what medication can be used, and what other body systems must be considered. Dogs with MUO often have no fever and no increased white blood cell counts. Patients with meningitis tend to have fever and increased white blood cell counts (neutrophilia).
Radiographs are taken in patients with neck pain to look for obvious bony and soft tissue changes. Magnetic Resonance Imaging (MRI, see MRI factsheet) is the golden standard in neuro-imaging and it is indicated in almost every patient with suspected brain or spinal cord disease. Both MRI and spinal taps require general anaesthetic. In patients with meningitis we often see diffuse swelling of the grey matter on MRI. In patients with MUO the grey matter, the white matter, the meningi and the spinal cord can be affected. >>

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<< Sampling of the cerebrospinal fluid (spinal tap) is necessary to further support the diagnosis of MUO and meningitis. Prior administration of steroid (prednisolone) medication may reduce the cells found in the tap and must be taken into account when interpreting the results of the spinal fluid analysis. A full diagnostic work-up also helps in ruling out other conditions that might present in a similar way but require different treatments. Examples of other causes include viral encephalitis, parasitic encephalitis, fungal encephalitis, strokes and tumours.

MRI is able to image the brain in such detail that it is considered nearly a confirming test for MUO and meningitis when combined with spinal fluid analysis. CT scanning is significantly less sensitive in diagnosing these conditions and CT scans can frequently give false negative results. The only way to confirm GME or meningitis with 100% certainty is by biopsy though, obviously, diagnostics do not get any more invasive than brain surgery. For this reason, 100% confirmation is can only achieved by post-mortem.

## TREATMENT:

The first part of treating patients with MUO and meningitis is to stabilise them. It should be emphasised that most patients with inflammatory CNS disease are emergency and critical care patients due to the acute and progressive nature of MUO and meningitis. Cardiac function and respiratory function can be impaired. The intra-cranial pressure can be raised and patients are often in a state of shock. Seizures themselves should be seen as emergencies and therefore patients of MUO who seizure should be considered critically ill.

The second part of treatment is immune suppression. The immune system needs to be aggressively suppressed in both patients with MUO and in patients with meningitis to control the inflammation. Therefore, immune-suppressive drugs are the mainstay in treating patients with MUO and meningitis. It is important to note that most patients will require to be hospitalised for 2-7 days as they need intensive veterinary care.

Treatment of Meningitis: Immune-suppression with corticosteroids (such as Prednisolone) is the choice of therapy for meningitis. Once the disease is controlled, one may begin to gradually drop the steroid dose until the minimum dose required to control the disease is reached. Most dogs need to be treated for about six months. A second drug is added to the medication in dogs with recurrent meningitis.

Treatment of MUO: Immune-suppression with corticosteroids combined with drugs (such as Cytarabine, Cyclosporine or Azathioprine) are for a period of at least six to twelve months. It is unusual for a patient with MUO to be able to fully discontinue medication. The prognosis with this combination treatment is vastly better compared to treatment with Prednisolone on its own. If seizures have been a manifestation of MUO, either disseminated or focal, anti-epileptic medication will be used to control the seizures. Ophthalmic GME also uses oral corticosteroids for therapy but may also employ topical ones. If glaucoma results from GME then therapy for this is necessary. Again, therapy for this result of GME is addressed in a standard way.

Our treatment protocol is as follows; Prednisolone long term starting at a high dose which can gradually be tapered Cytarabine (cytosine arabinose) injections for two days every three weeks. Cytarabine is a strong chemotherapy drug and specifically suppresses white blood cells). Cyclosporin is used as a third drug where there is a recurrence of the MUO whilst the patient is on Prednisolone and Cytarabine or where the side effects of these two drug are significant. Bloods tests should be taken regularly to check liver, kidney and bone marrow function.

Side-effects: The main side effects of medication are the classic steroid side effects (increased appetite, thirst, urination, lethargy and panting) and side effects related to the strong suppression of the immune system by the combination therapy. Signs of this are vomiting, diarrhoea, inappetence and pancreatitis.

## PROGNOSIS:

As mentioned above, the prognosis for patient with MUO can be poor. However, it is our experience that most patients will survive more than two years once they have been stabilised during the first few weeks on medication. The prognosis for most patients with meningitis is good.

## SUMMARY:

Inflammatory central nervous system disease (MUO and meningitis) is one of the most common neurological diseases in dogs. MUO and meningitis are generally not infectious. A definitive diagnosis is difficult and the main diagnostic tools are MRI and spinal fluid analysis. Early diagnosis is very important as this tend to improve long term outcome. Focal MUO generally has a better prognosis then multifocal MUO. Treatment with immune suppression should be aggressive and consistent of Prednisolone combined with a second drug like Cytarabine. Treatment should last at least six to twelve months and recurrence is c ommon.

Veterinary Hospital, Bradbury, Stockton-on-Tees TS21 2ES
T: 01388 777 770 | F: 0844 335 1831| info@wear-referrals.co.uk | www.wear-referrals.co.uk