



GRANULOMATOUS MENINGO-ENCEPHALOMYELITIS (GME) & MENINGO-ARTERITIS (MENINGITIS)

WHAT IS GME AND WHAT IS MENINGITIS?

Most people have never heard of GME, meningitis or any other form of central nervous system inflammation until they have a dog with progressive neurological disease. At Wear Referrals we see patients with GME or meningitis on a weekly 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 GME 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 GME and meningitis occur but they are thought to have an immune-mediated background. It is important to note that both GME and meningitis are generally not infectious diseases in contrast to meningitis in humans where they tend to be viral or bacterial on origin.

Granulomatous inflammation involves infiltration by cells called "mononuclear cells." These cells normally engulf and destroy debris. In GME, 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. GME 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 meninges.

THE CLINICAL PICTURE OF GME & MENINGITIS

The classical patient with GME 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 totally 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 (<1 year) large breed dogs. The Beagle is a smaller breed dog in which meningitis is frequently diagnosed. Some dogs can suffer from poly-arthritis (inflamed joints) at the same time as suffering from meningitis (Akita's, Bernese Mountain dog).

TYPES OF GME

There are different subtypes of GME: 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. There are some breed specific encephalitis types like necrotising encephalitis in the Yorkshire Terrier and Pug encephalitis.

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.

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.

Radiographs are taken in patients with neck pain to look for obvious bony and soft tissue changes. **Magnetic Resonance Imaging (MRI)** (*please see MRI download*) is the golden standard in neuro-imaging and it is indicated in almost every patient with



suspected brain or spinal cord disease. Tapping of the cerebrospinal fluid (spinal tap) is necessary to confirm the diagnosis of GME and meningitis. Both MRI and spinal taps require general anaesthetic. 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. In patients with meningitis we often see diffuse swelling of the grey matter on MRI. In patients with GME the grey matter, the white matter, the meninges and the spinal cord can be affected.

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. Some dogs with inflammatory disease of the central nervous system will also have inflammation of their joints (poly-arthritis).

MRI is able to image the brain in such detail that it is considered nearly a confirming test for GME and meningitis when combined with spinal fluid analysis. CT (CAT 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 normally only achieved by post-mortem.

TREATMENT

The immune system needs to be much suppressed in both patients with GME and in patients with meningitis. Therefore, immune-suppressive drugs are the mainstay in treating these patients. It is important to note that most patients with inflammatory CNS disease will require to be hospitalised for 2-7 days as they need intensive veterinary care.

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.

GME: Immune-suppression with corticosteroids combined with drugs as Cytarabine, Cyclosporine or Azathioprine) are for a period of at least six to twelve months. It is unusual for a patient with GME 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 GME, 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; no specific GME glaucoma therapy is needed.

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 GME whilst the patient is on Prednisolone and Cytarabine or where the side effects of these two drugs are too severe.

Bloods tests should be taken regularly to check liver, kidney and bone marrow function.

The main side effects of medication are the classic steroid side effects (increased appetite, increased thirst) 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 a patient with GME can be poor. However, it is our experience that some patients will survive more than two years once they have been stabilised during the first few weeks on medication. The prognosis in patients with meningitis is generally good.