Animal Medical Center of Seattle

Non-infectious Meningoencephalitis

MUE, Idiopathic tremor syndrome, and SRMA

Dr. Austin Kerns, DVM, MS, DACVIM (Neurology)

Abbreviations:

MUE - Meningoencephalitis of unknown etiology
GME - Granulomatous meningoencephalitis
NME - Necrotizing meningoencephalitis
NLE - Necrotizing leukoencephalitis
SRMA - Steroid responsive meningitis-arteritis

Summary:

- MUE is typically used as a broad umbrella term for most cases, but idiopathic tremor syndrome and SRMA are additional diseases that fall outside of MUE.
- These diseases are immune-mediated, and act clinically as auto-immune diseases
- Typical clinical summary:
    - MUE - Young to middle aged small/toy breeds with multifocal CNS disease. Seizures and vestibular signs are common. Treatment consists of steroids +/- additional immunosuppressives. Most dogs respond well to treatment, and live 1-3 years. Some dogs can be cured.
    - Idiopathic tremor syndrome - Young to middle aged small/toy breeds with acute onset tremors. Steroids alone typically control the disease, and many dogs can be cured.
    - SRMA - Medium to large breed dogs less than one year of age with acute onset lethargy, fever, and cervical pain. Typically neurologically normal otherwise. May have an inflammatory leukogram. Cervical radiographs should be performed to help rule out discospondylitis prior to immunosuppression. Steroids alone typically control the disease, and many dogs can be cured.

NB:

You will notice there are no references provided in this article. The reality is that there simply are not great references when it comes to a general clinical approach to these diseases. While some of the information is derived from a particular reference, most of it is from clinical experience and personal communication. This is also why any neurologist that would write this article would modify it to their liking based on their own anecdotes. I will happily provide references and further reading material to anyone who is interested.

Description and Nomenclature:

Non-infectious meningoencephalitides are a group of immune-mediated diseases found in dogs. Other common terms include sterile meningoencephalitis or inflammatory brain disease. While an auto-antigen has not been well established in these diseases to classify them as true auto-immune diseases, they behave clinically as auto-immune diseases both in their presentation and response to treatment, and referring to them as such typically makes owner education easier. A long list of infectious diseases have been evaluated in an attempt to identify an underlying cause, but to no avail.

Since first being described in the 1980s, a variety of terms have been used to describe various forms of these diseases, mainly as a result of our poor understanding of their etiology and pathophysiology. In this case the general rule, that the more names a disease process has the less we know about it, holds true. The earliest

and best described diseases include granulomatous meningoencephalitis (GME), necrotizing meningoencephalitis (NME), and necrotizing leukoencephalitis (NLE). GME, NME, and NLE have all more recently been classified under the umbrella term meningoencephalitis of unknown etiology (MUE). Because GME, NME, and NLE are all histopathologic diagnoses (i.e. diagnosed with brain biopsy), MUE is used as a broad placeholder in most clinical situations, as brain biopsies to confirm histologic diagnoses are rarely performed. Thus, MUE is the preferred terminology in nearly all cases where a non-infectious meningoencephalitis is suspected. Two other relatively common non-infectious meningoencephalitdes that do not fall under MUE include steroid responsive meningitis-arteritis (SRMA) and idiopathic tremor syndrome (aka immune-mediated cerebellitis or “little white shaker disease”). A small list of other rare diseases will not be discussed here.

Etiology:

MUE, SRMA, and idiopathic tremor syndrome appear to be immune-mediated diseases without any apparent trigger. There is no good evidence to suggest vaccination or particular medications are correlated or causative. Anecdotally there may be a regional difference in response to treatment and prognosis.

Clinical Approach:

Listed below is the typical presentation, exam findings, diagnostic findings, treatment regimen, and prognosis for these cases. Keep in mind that these are generalities.

MUE:

Signalment

Most dogs present between 6 months and 8 years of age, without sex predilection. Small/toy breeds represent the vast majority of cases. Genetic predispositions have been identified in the Pug and Maltese. Other common breeds include Yorkshire terriers, Chihuahuas, French Bulldogs, Papillons, Shih Tzus, Toy Poodles, and Coton du Tulears. Recently, MUE has been identified in multiple medium and large breed dogs, and can occasionally be diagnosed in older small breeds.

History

A wide range exists, anywhere from acute onset of severe signs, to waxing and waning clinical signs over the course of weeks to months. Seizures and vestibular signs (head tilt, nystagmus, ataxia) are common.

Exam

Seizures and vestibular signs (head tilt, nystagmus, ataxia) are common. Because the disease can affect every part of the CNS, any neurologic deficit is possible. However, for this reason, multifocal CNS disease (e.g. seizures and vestibular disease simultaneously) should immediately put MUE at the top of your differential list with the appropriate signalment. Occasionally these dogs will have cervical pain along with their neurologic deficits due to cervical meningitis.

Diagnostics

Extra-CNS diagnostics are typically normal. Thus, significant abnormalities on extra-cranial work-up that correlate with clinical presentation may suggest other etiologies. For example, while a mildly elevated neutrophil count is expected for a stressed patient, a moderate or severe neutrophilia is not consistent with MUE, and other infectious/inflammatory conditions should be considered.

MRI and spinal tap, +/- negative CNS infectious disease testing are typically required to confirm a diagnosis.

Treatment
Steroids initially at an immunosuppressive dose, then taper gradually over the course of 3-6 months. There is some evidence to suggest that adding another immunosuppressive medication early on in treatment may improve outcome, but there is no good evidence that any one drug is superior to another. This choice is typically based on patient size, medication cost, and frequency of administration.
Many neurologists will use prednisone + cytarabine, as cytarabine crosses the blood brain barrier and targets lymphocytes which are one of the primary immune cell types found in the CNS of patients with MUE, but a nearly endless combination of medication regimens have been reported. Other commonly used medications include cyclosporine, mycophenolate, leflunomide, and azathioprine.

Prognosis
Prognosis is extremely variable, and the most important predictor of prognosis is initial response to treatment. There seems to be little correlation between severity of CNS disease at presentation and long-term prognosis. While most patients will respond well to treatment, many will require life-long treatment with at least one medication as relapses are common. Generally speaking, most dogs live 1-3 years before they relapse and succumb to the disease or succumb to side effects of chronic immunosuppression. Occasionally dogs are cured.

Idiopathic tremor syndrome:
Signalment
Young to middle aged small breeds, similar to MUE.

History
Acute onset tremors.

Exam
Relatively fine generalized tremors are the most prominent finding. The eyes may also have erratic uncoordinated movements, referred to as opsoclonus. These patients may be hyperthermic due to their constant tremors.

Diagnostics
Similar to MUE.

Treatment
Steroids initially at an immunosuppressive dose, then taper gradually over the course of 3-6 months. Additional immunosuppressive medication is rarely needed. These dogs may benefit from injectable and/or oral benzodiazepines to help minimize tremors at presentation and in the initial days of treatment until tremors subside.

Prognosis
Most dogs will have their signs controlled with steroids alone, and many can be cured.

SRMA:
Signalment

Nearly all dogs present less than 2 years of age, with most presenting less than 1 year of age. Commonly found in the “B” breeds, including the Boxer, Bernese Mountain Dog, and Beagle. However, SRMA has been found in many medium to large breed dogs.

History
Acute onset lethargy, fever, and cervical pain.

Exam
Fever and cervical pain are typically the only findings. It is uncommon to have any neurologic deficits, though mild proprioceptive deficits may occasionally be found.

Diagnostics
An inflammatory leukogram may be found in addition to a fever, as this disease tends to affect patients systemically. This is one of a few cases where cervical radiographs are indicated, as discospondylitis is the main other differential for this clinical picture. MRI and spinal tap, +/- negative CNS infectious disease testing is typically required to confirm a diagnosis. However, spinal tap alone may be sufficient.

Treatment
Steroids initially at an immunosuppressive dose, then taper gradually over the course of 3-6 months. Additional immunosuppressive or pain medication is rarely needed.

Prognosis
Most dogs will have their signs controlled with steroids alone, and many can be cured.

Animal Medical Center of Seattle
Emergency/Critical Care Oncology Dermatology Internal Medicine Interventional Radiology
Dentistry Neurology Surgery Ophthalmology Hyperbaric Oxygen Therapy
17518 15th Ave NE Suite B., Shoreline, WA 98155
P: (206) 204-3366 l **F**: (206) 204-3858
www.AnimalMedicalSpecialists.com