

Canine Encephalitis

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Definitions

- Encephalitis: Inflammation of the brain
- Meningitis: Inflammation of the meninges
- Myelitis: Inflammation of the spinal cord

Neurodiagnostic Tools

- Neurologic examination
- Blood and urine tests
- Radiographs (x-rays)
- Cerebrospinal fluid evaluation
- Infectious disease titers/PCR
- Advanced diagnostic imaging
 - Computed tomography (CT)
 - Magnetic resonance imaging (MRI)



Neurologic Examination

- Attitude and responsiveness
- Cranial nerve examination
- Gait
- Proprioception (position sense)
- Spinal reflexes
- Spinal pain

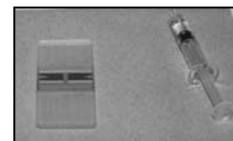


CSF Risks and Drawbacks

- Penetration of neural tissue
 - Routine with collection from LC
 - At CMC → enter brainstem (vestibular signs, respiratory compromise)
- Shifts of intracranial tissue (↑ ICP)
 - Brain herniation
 - Death
 - Pre-emptive imaging and mannitol

CSF Analysis

- Cell counts
- Cytology
- Protein



CSF Analysis

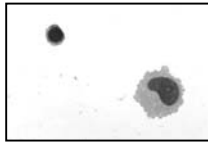
- ⊖ Normal CSF
 - ⊖ Small numbers white blood cells
 - ⊖ 0-5 cells/ μ l (CMC), 0-8 cells/ μ l (LC)
 - ⊖ Lymphocytes
 - ⊖ Large mononuclear phagocytes (macrophages)
 - ⊖ No red blood cells
 - ⊖ Protein
 - ⊖ Less than 20-25 mg/dl (CMC)
 - ⊖ Less than 30-40 mg/dl (LC)

CSF Cell Counts

- ⊖ \uparrow RBC count
 - ⊖ Usually iatrogenic (obvious at time of collection)
 - ⊖ Occasionally CNS hemorrhage
 - ⊖ If old, xanthochromia may be present
- ⊖ \uparrow WBC count
 - ⊖ Meningoencephalitis
 - ⊖ Neoplasia
 - ⊖ Acute trauma

CSF Cytology

- ⊖ Normal
 - ⊖ Lymphocytes and mononuclear phagocytes
- ⊖ Abnormal
 - ⊖ Neutrophils
 - ⊖ Eosinophils
 - ⊖ Neoplastic cells
 - ⊖ Infectious organisms
 - ⊖ Vacuolation of phagocytes
 - ⊖ Other material (e.g. myelin)



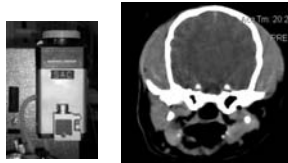
CT Risks and Drawbacks

- ⊖ General anesthesia
 - ⊖ Health hazard
 - ⊖ Limited patient access during procedure
- ⊖ X-ray radiation
 - ⊖ Limited imaging of brainstem
 - ⊖ "Beam hardening" artifact
- ⊖ Cost



CT Usefulness

- ⊖ Very good resolution of bone
 - ⊖ Much better than plain x-rays
- ⊖ Visualization of acute hemorrhage
- ⊖ Compatibility with anesthetic machines and monitoring devices
- ⊖ No contraindication with pacemakers, medical implants
- ⊖ Rapid image acquisition



MRI Risks and Drawbacks

- ⊖ General anesthesia
- ⊖ Very strong magnetic field
 - ⊖ Not safe for pacemakers
 - ⊖ Other metal implants can be troublesome
 - ⊖ Not compatible with standard anesthesia machines or monitoring equipment

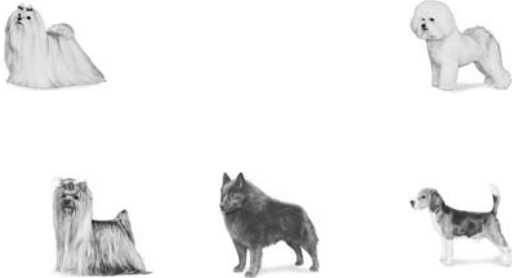
MRI Advantages/Usefulness

- Indications
 - Any disease of the nervous system
 - No beam hardening artifact in brainstem
- Superior image resolution and sensitivity
- Multiple plane imaging
- Multiple protocols available

Encephalitis Terminology

- Little white shaker disease
- Steroid-responsive meningitis-arteritis
- Granulomatous meningoencephalitis
- Necrotizing meningoencephalitis
- Steroid-responsive meningoencephalitis
- Meningoencephalitis of unknown etiology

Little White Shaker Syndrome



Little White Shaker Syndrome

- Sudden onset of tremors all over body
- Worsens with excitement, handling, locomotion
- Improves with relaxation, sleep
- Rare seizures

Steroid-Responsive Meningitis-Arteritis

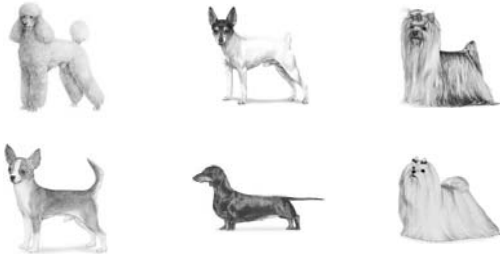
Mainly large breeds
Typically neck pain without deficits
Neutrophilic inflammation in CSF



Granulomatous Meningoencephalitis (GME)

- Brainstem, cerebellar, spinal cord more involved than forebrain
- Mononuclear cells or mixed cells in CSF
- Initially responsive to prednisone but usually becomes resistant

Granulomatous Meningoencephalitis (GME)



Necrotizing Meningoencephalitis (NME)

A Necrotizing Meningoencephalitis of Pug Dogs 1989
 D. R. CORDY AND T. A. HOLLIDAY
 Department of Pathology and Department of Surgery, School of Veterinary Medicine,
 University of California-Davis, Davis, CA

Necrotizing Meningoencephalitis of Maltese Dogs 1995
 I. H. STALLS, B. CHADWICK, B. DAYRELL-HART,
 B. A. SUMMERS, AND T. J. VAN WINKLE
 Laboratory of Pathology (IHS, TVW) and Department of Clinical Studies (BD), School of Veterinary Medicine,
 University of Pennsylvania, Philadelphia, PA, Department of Pathology,
 School of Veterinary Studies, Murdoch University, Perth, WA, Australia (BC), and
 Department of Pathology, New York State College of Veterinary Medicine,
 Cornell University, Ithaca, NY (BAS)

Necrotizing Meningoencephalitis (NME)

- Forebrain more involved than brainstem, cerebellum, spinal cord
- Seizures, altered awareness, blindness, circling, weakness

Necrotizing Meningoencephalitis (NME)

- Diagnosis
 - Advanced imaging
 - Mononuclear cells in CSF
- Response to medications unclear
 - Often unresponsive to prednisone
 - May respond to more potent immunosuppressive medications

Necrotizing Meningoencephalitis (NME)



Necrotizing Leukoencephalitis (NLE)

Like NME but little meningeal involvement and more brainstem signs

Necrotizing encephalitis in Yorkshire terriers

A. Tipold, R. Fatzet, A. Jaggy, A. Zurbriggen and M. Vandevelde
 Institute of Animal Neurology, University of Bonn, Bismarckstrasse 109 a, D-53105 Bonn, Switzerland



1993

Treatment

- ↳ Infectious disease
 - ↳ Antibiotics
 - ↳ Antifungals
 - ↳ Anti-rickettsials
 - ↳ Anti-inflammatory therapy
 - ↳ Steroids



Treatment

- ↳ Little white shakers
 - ↳ Steroids (prednisone)
 - ↳ Diazepam (valium)



Treatment

- ↳ GME, NME, MUE
 - ↳ Antibiotics while awaiting infectious tests
 - ↳ Anti-inflammatory vs. immunosuppression
 - ↳ Steroids

Immunosuppression

- ↳ Immunosuppressives
 - ↳ Cyclosporine (Sandimmune, Neoral)
 - ↳ Leflunomide
 - ↳ Mycophenolate mofetil (Cellcept)
- ↳ Anti-cancer drugs
 - ↳ Cytosine arabinoside (Cytosar, Ara-c)
 - ↳ Procarbazine
 - ↳ Lomustine (CCNU)

Immunosuppression

- ↳ Risks and side effects
 - ↳ Worsening infectious disease
 - ↳ Myelosuppression (low white blood cells)
 - ↳ Secondary infections
 - ↳ Gastrointestinal
 - ↳ Vomiting, diarrhea

Prednisone

- ↳ Risks and side effects
 - ↳ Increased risk of secondary infections
 - ↳ Increased thirst and urination
 - ↳ Increased hunger
 - ↳ Weight gain
- ↳ Muscle wasting
- ↳ Coagulation problems
 - ↳ Lung clots

Prognosis

- Little white shakers - Good - excellent
- GME - guarded - poor
- NME - poor
- MUE - variable

Challenges & Problems

- No idea of underlying cause
- Genetic influence
- Occult infection?
- Autoimmune disease?
- Triggers?

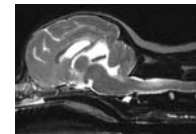


Challenges & Problems

- Poor sense of underlying disease course
 - GME
 - NME

Challenges & Problems

- Sorting out multiple disease problems
 - Encephalitis
 - Chiari-like malformation (COMS)
 - Stroke
 - Liver shunts



Challenges & Problems

- Limitations current diagnostic tests
 - Imaging
 - Equivocal CSF results
 - CSF not absolutely specific for encephalitis

The Way Forward...

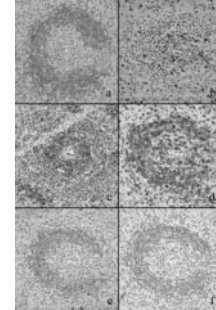
- Diagnostic tests
 - Diagnostic imaging
 - Biopsy systems
 - Additional organisms
 - Genetic based test
 - Causative gene
 - Susceptibility genes

The Way Forward...

- Treatment
 - Prednisone vs. other immunosuppressive and anti-cancer drug trial
 - Immunomodulatory therapy
 - Plasma exchange
 - Intravenous immunoglobulin
 - Targeted molecular therapy

Mariani Lab

- Characterization of immune response
 - Blood, spinal fluid, tissue samples
 - Design better diagnostic tests
 - Tailor choice of therapies



Mariani Lab

- Define genetic predisposition
 - Linkage studies
 - Association studies
 - Haplotype analysis
 - Affected and unaffected dogs

How You Can Help...

- Support encephalitis research
 - AKC Canine Health Foundation
 - CREATE Fund (NCSU)
- We need:
 - Blood samples, CSF, tissue from affected dogs
 - DNA from affected and unaffected dogs
 - Blood samples
 - Cheek swabs



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Questions?



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