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/μl (CMC)
    - 0-8 cells/μl (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

- ↑ RBC count
  - Usually iatrogenic (obvious at time of collection)
  - Occasionally CNS hemorrhage
    - If old, xanthochromia may be present
- ↑ 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
- X-ray radiation
  - Health hazard
  - Limited patient access during procedure
- 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**

- 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)

Necrotizing Meningoencephalitis (NME)

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

Necrotizing Leukoencephalitis (NLE)

Like NME but little meningeal involvement and more brainstem signs

Necrotizing Meningoencephalitis of Maltese Dogs

Necrotizing Meningoencephalitis of Pug Dogs

1989

1995

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

- Infectious disease
  - Antibiotics
  - Antifungals
  - Anti-rickettsial
  - Anti-inflammatory therapy
  - Steroids

**Treatment**

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

**Immunosuppression**

- 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
  - Muscle wasting
  - Coagulation problems
  - Lung clots
  - Increased risk of secondary infections
  - Increased thirst and urination
  - Increased hunger
  - Weight gain
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
  - Immumodulatory 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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