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MOVEMENT DISORDERS AND CNS INFECTION/INFLAMMATION

October 25th, 2018
Outline

- CNS infections causing movement disorders
  - Viral infections
    - HIV/JC
    - West Nile virus
    - Viral parkinsonism
  - Bacterial infections
    - Whipple’s disease
  - Parasitic infections
    - Toxoplasmosis
    - Cysticercosis
  - Prion diseases
    - CJD

- CNS inflammation causing movement disorders
  - Tremor in multiple sclerosis
  - Autoimmune ataxias
  - Autoimmune chorea
  - LGI1 encephalitis
  - Anti-NMDArAb encephalitis
  - Anti-GAD syndromes
  - Post-infectious movement disorders
    - Sydenham’s chorea
    - Post infectious ataxia
    - Post encephalitic parkinsonism
Viral CNS infections
HIV-related movement disorders

- 3% of HIV+ patients
- ~50% AIDS develop tremor or parkinsonism

Mechanisms:
- Opportunistic infections
- Direct effect of HIV virus
- Use of dopamine blockers

Different movements have been described:
- Hemichorea-hemiballism
- Dystonia
- Chorea
- Myoclonus
- Tics
- Paroxysmal dyskinesias
- Parkinsonism

HIV demographics in Africa

Akinetic-rigid syndrome in HIV-related PML

- JC virus (DNA polyomavirus)
- Present worldwide
- Asymptomatic infection in childhood
- Reactivates when immunosuppressed
- Tropism for oligodendrocytes

Singer, et al. Movement Disorders; 8:1, 1993. 113-116
WNV encephalitis causing opsoclonus-myoclonus

- Opsoclonus-myoclonus
  - 1:10,000,000/year
  - 2-3% of children with neuroblastoma

- Other causes of OM:
  - Celiac disease
  - Breast/Small Cell CA
  - Anti-Ri

- Treatment
  - Steroids
  - IVIG
  - Rituximab
Viral parkinsonism

<table>
<thead>
<tr>
<th>Virus</th>
<th>Family</th>
<th>Species</th>
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<tbody>
<tr>
<td>DNA</td>
<td>Herpesviridae</td>
<td>Herpes simplex virus</td>
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<td>Epstein-Barr virus</td>
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<td>Cytomegalovirus (CMV)</td>
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<td>Varicella zoster virus (VZV)</td>
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<td>RNA</td>
<td>Bornaviridae</td>
<td>Borna disease virus</td>
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<td>Picornaviridae</td>
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<td>Retroviridae</td>
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<td>Human Immunodeficiency Virus (HIV)</td>
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<td>West Nile virus</td>
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<td></td>
<td>Japanese encephalitis B virus</td>
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<td>St. Louis Virus</td>
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</table>
Bacterial CNS infections
Whipple’s Disease

- **Tropheryma whippelii**
- **Symptoms:**
  - GI: arthralgias, weight loss, abdominal pain and diarrhea.
  - Neurologic: cognitive impairment, supranuclear gaze palsy, ataxia, **oculomasticatory myorhythmia**.
- **Diagnosis:** Duodenal biopsy.

Parasitic CNS infections
CNS Toxoplasmosis

- Presenting symptoms
  - Fever
  - Headache
  - Altered mental status
  - Focal neurologic complaints or seizures

- Supporting laboratory findings
  - Toxoplasma antibodies
  - CD4 counts <100 cells/microL

- Typical CNS lesions are ring-enhancing at
  - Parietal or frontal lobes
  - Thalamus
  - Basal ganglia*
  - Corticomedullary junction

- CNS lymphoma is main differential diagnosis

CNS Toxoplasmosis

Toxoplasmosis Prevalence

http://retinavitreous.com/diseases/toxoplasmosis.php
Hemichorea in a patient with AIDS/CNS Toxoplasmosis
Hemichorea-hemiballismus in a patient with AIDS/CNS Toxo

Enhancing lesion of the right STN
Focal dystonia in a patient with AIDS/CNS Toxoplasmosis

Contrasted computed tomography scan showing enhanced toxoplasmosis abscesses in right lenticular nucleus and left temporal cortex (arrows) (A) and right thalamus (arrow) (B).
Neurocysticercosis

- Larval stage (metacestode) of the Taenia solium
Neurocysticercosis

Intraparenchymal (Epilepsy)

Extraparenchymal

Intraventricular (ICP, hydrocephalus)

Subarachnoid (arachnoiditis)

Spinal (Myelitis or radiculitis)

Ocular

Parkinsonism in midbrain neurocysticercosis

Cranial magnetic resonance scan (February 18). A: A postgadolinium axial T1-weighted image shows enhancement in the periaqueductal gray matter (long arrow) and the medial ventral midbrain (short arrow). B: A midsagittal section reveals contiguous areas of nodular (short arrow) and peripheral, cyst-like enhancement in the fourth ventricle. The enhancement in the periaqueductal region (long arrow) and ventral mesencephalon is also seen. C: An axial section through the medulla shows the cystic lesion within the fourth ventricle.
Facial myokimia in pontine neurocysticercosis
Prion diseases
Creutzfeldt-Jakob disease

- 100% invariably fatal
- 250-300 cases/year in the US

CAUSES

- Sporadic, 85%
- Familial, 14%
- Infectious, 1%

https://www.cdc.gov/prions/cjd/about.html
Venneti. DOI:10.1016/j.cll.2009.11.002x
Diagnosis of CJD

1Hz periodic discharges

Typical MRI Changes

Venneti. DOI:10.1016/j.cll.2009.11.002x
Diagnosis of CJD

Quantitative real-time quaking-induced conversion

Spongiform changes on brain biopsy
CNS Inflammatory diseases featuring Movement Disorders
Autoimmune Movement Disorders
Autoimmune ataxia

- Often paraneoplastic
- Most frequent cancers:
  - Lung (small cell)
  - Ovarian
  - Breast
  - Lymphoma
- Most frequent Abs:
  - Anti-Yo
  - Anti-Hu
  - Anti-Ri
  - Anti-Ma

Paraneoplastic cerebellar degeneration in a patient with Hodgkin’s lymphoma with anti-Tr antibodies
# Autoimmune Chorea

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<tr>
<th>Paraneoplastic</th>
<th>Idiopathic</th>
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<tr>
<td>CRMP-5</td>
<td>CASPR2</td>
</tr>
<tr>
<td>ANA</td>
<td>ANA</td>
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<tr>
<td>aPL</td>
<td>aPL</td>
</tr>
<tr>
<td>TPO</td>
<td>TPO</td>
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<tr>
<td>ENA</td>
<td>ENA</td>
</tr>
<tr>
<td>RF</td>
<td>ASO</td>
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<tr>
<td>GAD65</td>
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<td>VGCC P/Q</td>
<td>dsDNA</td>
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<table>
<thead>
<tr>
<th></th>
<th>Paraneoplastic group (n = 14)</th>
<th>Idiopathic group (n = 22)</th>
<th>p Value</th>
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</thead>
<tbody>
<tr>
<td>Age, median</td>
<td>72 y</td>
<td>45 y</td>
<td>0.001</td>
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<tr>
<td>Male sex</td>
<td>10/14</td>
<td>5/22</td>
<td>0.006</td>
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<tr>
<td>Moderate or severe chorea</td>
<td>9/11</td>
<td>9/22</td>
<td>0.06</td>
</tr>
<tr>
<td>Generalized onset</td>
<td>8/14</td>
<td>8/22</td>
<td>0.307</td>
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<tr>
<td>Weight loss (±4 kg)</td>
<td>10/14</td>
<td>7/22</td>
<td>0.02</td>
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<tr>
<td>Coexisting neurologic disorder</td>
<td>12/14</td>
<td>14/22</td>
<td>0.25</td>
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<tr>
<td>Coexisting peripheral neuropathy*</td>
<td>6/14</td>
<td>1/22</td>
<td>0.008</td>
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<tr>
<td>Spontaneous remission/improvement</td>
<td>8/14</td>
<td>12/22</td>
<td>1.00</td>
</tr>
</tbody>
</table>

LGI1 encephalitis

- Limbic encephalitis
  - Confusion
  - Disorientation
  - Seizures
- Medial temporal lobe inflammation
- Seizures semiology
  - Medial temporal lobe events
  - Bradycardia
  - Piloerection
  - Faciobrachial dystonic seizures (FBDS)

Watson, et al. DOI: https://doi.org/10.1212/CPJ.000000000000016
Anti-NMDAr Ab encephalitis

- First described @ UPenn in 2007
- More common among young women
- Associated with ovarian teratomas
- Symptoms
  - Paranoia, hallucinations
  - Cognitive changes
  - Aphasia
  - Movement Disorder
  - Seizures
  - Dysautonomia

https://www.med.upenn.edu/autoimmuneneurology/nmdar-encephalitis.html
Anti-GAD syndromes

- Stiff person syndrome was first described in 1956.
- GAD antibodies were documented in association with SPS in 1988.
- The spectrum of anti-GAD syndromes includes:
  - Stiff person syndrome
  - Stiff limb/trunk syndromes
  - Cerebellar ataxia
  - PERM
- Comorbid autoimmune disease and malignancy must be excluded.

https://infodiabet.files.wordpress.com/2012/04/reduction-of-gaba.jpg
Anti-GAD syndromes

Management

1. Exclude false positives results
   • Confirm titer levels
   • Check antibody levels in the CSF
2. Rule out malignant disease
3. Treatment
   • No RCTs or Class I evidence
   • Recommendations based on expert consensus
   • Medications include:
     • Pulse steroids
     • IVIG
     • Rituximab
Postinfectious Movement Disorders
Sydenham’s chorea

- Most common acquired chorea in childhood
- Mimicry against tubulin and lysoganglioside
- Chorea 1-8 mos after group A strep infection

**Testing**
- ASO titer (peaks 4 weeks after the infection)
- antideoxyribonuclease (anti-DNAse) B titer

**Treatment**
- prednisone 1 mg/kg/d x 2 wks followed by a 2-3 wk taper

Worldwide epidemiology of acute rheumatic fever

Postinfectious ataxia

- **Postinfectious ataxia**
  - Mean age of presentation: 5 +/- 4 yrs
  - Prodrome to ataxia onset: 9 +/- 7 days
  - Prodromal febrile illnesses are common
  - Patients exhibit nystagmus and dysmetria
  - Full recovery in 2-3 weeks

Common causes of postinfectious ataxia:

- Varicella: 31%
- Mumps: 25%
- Nonspecific viral illness: 16%
- Mycoplasma: 20%
- Unknown: 5%

Postencephalitic parkinsonism

- von Economo’s disease
- 1916-1925
- Unclear link to the Spanish Flu Pandemia
- Pharyngitis followed by a sleep disorder, movement disorders and psychiatric disturbances
THANK YOU!