CNS INFECTIONS WITH MOVEMENT DISORDERS SYMPTOMATOLOGY

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To disseminate knowledge and promote research to advance the field of Movement Disorders

http://www.movementdisorders.org
Objective

Highlight the spectrum of CNS infections manifesting movement disorders phenomenology
Outline

- Overview – some basics of movement disorders
- Overview of aetiologies of movement disorders
- Infectious causes of movement disorders
- Parainfectious movement disorders
- General approach/summary
Definition

Neurologic syndromes in which there is either an excess of movement or a paucity of voluntary and automatic movements, unrelated to weakness or spasticity

- Hyperkinesias (aka dyskinesias)
- Hypokinesias
Hypokinesias

- Parkinsonism
- Apraxia
- Blocking (holding) tics
- Cataplexy and drop attacks
- Catatonia, psychomotor depression and obsessional slowness
- Freezing phenomenon
- Hesitant gaits
- Hypothyroid slowness
- Rigidity
- Stiff muscles
Hyperkinesias

- Tremor
- Dystonia
- Chorea/Ballism
- Athetosis
- Hemifacial spasm
- Myoclonus
- Ataxia/asynergia/dysmetria
- Tics
- Abdominal dyskinesias
- Akathitic movements
- Hyperekplexia
- Jumping disorders
- Jumpy stumps
- Moving toes and fingers
- Myokymia and synkinesis
- Myorhythmia
- Paroxysmal dyskinesias
- Periodic movements in sleep
- REM sleep behavior disorder
- Restless legs
- Stereotypy

Localization of movement disorders

- Structural lesions
  - Functional (neurochemical) abnormalities
Define the dominant movement disorder

Identify associated neurological features

Identify associated non-neurological features

Clinically based syndrome

Diagnostic work-up

Presence of one or more movement disorders?

Identify all subtypes present

Aetiologies of movement disorders

- Primary
  - Neurodegenerative

- Hereditary

- Secondary
  - Metabolic
  - Vascular
  - Tumors
  - Trauma
  - Infections
  - Inflammatory
  - Demyelinating
  - Paraneoplastic
  - Toxins
Infection-related MD mechanisms

- Direct consequence of active infection in relevant cerebral structures
  - Movement disorder

- Delayed immune-mediated process secondary to previous infection
  - Movement disorder
Characteristics

~ 20% (1/5th) of all secondary movement disorders

Scenario: infectious or post-infectious

Hypokinetic or hyperkinetic, single or mixed

Commoner types: dystonia, hemichorea/hemiballism, tremor, tics, myoclonus, paroxysmal dyskinesias, parkinsonism

Aetiologies:
viral, bacterial, parasitic, fungal, prion
Characteristics ii

- **Demographic profile**
  - Typically young onset (<20), but any age; based on distribution of cause

- **Time from infection to MD**
  - Acute or subacute onset or delayed by months to years
  - Typically about 6 weeks from onset of infection (but depends on cause)

- **Phenomenology**
  - Dystonia (~50% ± choreoathetosis); mixed (~23%); parkinsonism (~15%); generalized (~60%); also varies by aetiology (predilection)

** Data based on few published case series (mainly from Asia)
Aetiologies

Viral:
HIV, Others

Bacterial

Parasitic

Fungal

Prion-related:
Kuru, CJD
Some considerations....

- Fever and constitutional symptoms may be absent
- Evidence of infection may be remote
- Immune status may be normal or impaired
- Immunosuppression goes beyond associated HIV infection
- Readily available imaging (CT) may be normal
- Travel history, dietary habits, risk factors require eliciting
- The MD may be the major presenting complaint or masked by other neurologic or systemic features
HIV/AIDS-associated MD

- Clinically relevant MD in ~3% only (but on prospective follow up~50%)
- Most common hyperkinesias: hemiballism/hemichorea and tremor
- May have other associated neurological problems

Aetiologies

- Opportunistic infections and diseases
  - (esp. toxoplasmosis, T. pallidum, Crypt. neoformans, PML, primary lymphoma)
- Direct effect (HIV encephalopathy, dopaminergic dysfunction) → parkinsonism
- Drug induced e.g. antidopaminergic drugs, enhanced physiologic tremor
HIV/AIDS-associated MD

- Hyperkinetic movement disorders
  - Hemichorea-hemiballism most often
    - Acute onset in known AIDS or first presenting feature
  - Generalized or focal dystonia
  - Paroxysmal dyskinesias (non-specific trigger)
  - Myoclonus: action cortical, spinal or peripheral segmental
  - Others: oculomasticatory myorrhythmia (Whipple’s), tics, akathisia, NMS

- Parkinsonism and tremor – usually due to HIV encephalopathy
Cryptococcomas in the basal ganglia
HIV/AIDS-associated MD ii

**Treatment**

- Specific to suspected aetiology (e.g. sulfadiazine + pyrimethamine in toxo)
- HAART*
- Symptomatic treatment
  - reserpine, valproic acid or tetrabenazine for hemiballism-hemichorea
  - Tremor: levodopa, anticholinergics, propranolol, clonazepam, etc
  - Parkinsonism: levodopa/carbidopa (Efficacy)

*HAART drugs with CNS activity may prevent MD or improve symptoms (zidovudine, stavudine, lamivudine, abacavir, nevirapine, efavirenz, indinavir)
## MD associated with other viral infections

<table>
<thead>
<tr>
<th>Hyperkinetic movement</th>
<th>Virus</th>
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</thead>
<tbody>
<tr>
<td>Tremor</td>
<td>WNV (static, kinetic)</td>
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<tr>
<td></td>
<td>Kuru (cerebellar)</td>
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<tr>
<td></td>
<td>JEV (postural, rest, intermittent)</td>
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<td></td>
<td>CJD (rest, postural)</td>
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<tr>
<td>Chorea</td>
<td>Variant CJD, WNV, Kuru, HSV, JEV</td>
</tr>
<tr>
<td>Dystonia</td>
<td>WNV, JEV, Variant CJD,</td>
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<tr>
<td>Myoclonus</td>
<td>Variant CJD, WNV, Kuru, JEV</td>
</tr>
</tbody>
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WNV – West Nile virus  
CJD – Creutzfeldt-Jakob disease  
JEV – Japanese encephalitis virus  
HSV – Herpes simplex virus
MD associated with tuberculosis

- **Mechanisms**
  - Space occupying lesion
  - Vascular (stroke-like)
  - Inflammation

- **Phenomenology**
  - Hemichorea
  - Unilateral parkinsonism
  - Others

- **Treatment**
  - Antituberculous therapy
  - Surgery (if amenable)
  - Steroids
  - Antituberculous therapy
MD associated with neurocysticercosis

- Accidental ingestion of Taenia solium eggs
- Subacute onset typically
- Bilateral but often asymmetric
- Chorea and dystonia: closely aligned with pathology
- Treatment:
  - Anthelmintic (albendazole)
  - May require steroid, surgery, symptomatic tx of the MD
Neurocysticercosis

T1 MRI

T2 MRI
MRI findings in MD of infectious cause

- Abnormal in ~80%
- Signal changes in thalamus (~1/2)
  - Common location in cases with dystonia
- Signal changes in other parts of basal ganglia
- Signal changes in midbrain (~4%)

*Data based on few published case series (mainly from Asia)*
Parainfectious (autoimmune) MD

Hyperkinetic or hypokinetic

Mechanisms

• Molecular mimicry (infectious agents v. neural agents)
• Host susceptibility (HLA allelic differences)
Sydenham chorea

- Onset 8-9 years; mostly girls
- Autoimmune response to group A β-hemolytic streptococcal infection (often pharyngitis)
- Leading cause of paediatric chorea globally
- Isolated or with other acute rheumatic fever syndrome features (arthritis, carditis, skin rash)
- 4-8 weeks after GABHS
Sydenham chorea – clinical features

- Acute onset chorea (20% hemichorea onset, generalized in most)
- Chorea lasts 2-3 months then abates (may last up to 2 years)
- Motor impersistence, hypotonia, tics, abnormal EOMs
- Behavioral abnormalities (anxiety, OCD, depression, disruptive behavior)
- May recur (also in pregnancy – chorea gravidarum)
Sydenham Chorea – lab diagnosis

- **Laboratory diagnosis**
  - ↑ antistreptolysin O titer
  - ↑ antideoxyribonuclease B
  - Positive streptozyme
  - Throat culture for streptococcus pyogenes

- **MRI** – normal or signal changes in basal ganglia
Sydenham Chorea – treatment

- Antibiotics
- Valproic acid
- Neuroleptics
- Anti-depressant and anti-anxiety medications
- Immunotherapy – steroids, plasmapharesis, IVIG in severe cases
Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection

- Sudden psychiatric onset
- Obsessive compulsive disorder ± tics, other motor abnormalities
- Inconsistent evidence of streptococcal infection or immune response
- ? Nonexistent → Paediatric Acute-onset Neuropsychiatric Syndrome (PANS)
- Symptomatic treatment
Other para-infectious MD

- Opsoclonus-myoclonus syndrome
  - Hep C, mycoplasma, dengue, influenza, HIV
- Dystonia (generalized, segmental; infantile bilat. striatal necrosis)
- Mixed: Anti-NMDA receptor encephalitis (post HSE); HIV
- Parkinsonism (post viral)
- Ataxia (post– varicella, enterovirus, EBV; mycoplasma)
- Infantile bilat. striatal necrosis post group A beta hemolytic strept. infxn

**Treatment:** immunotherapy; symptomatic therapy
General approach

- High index of suspicion in acute/subacute-onset movement disorders
- Onset may be more insidious and associated infection may be remote
- Clinical evaluation: isolated MD, mixed MD, MD + other neurologic features, MD + other systemic features ± other neurologic features to determine the syndrome
- Additional diagnostic evaluation if indicated to explore aetiology further (blood labs, brain imaging, EEG, etc)
- Treatment approach:
  - typically combination of symptomatic, disease specific (infection-targeted) and immunomodulatory (if indicated)