Overview of MSA, PSP and CBS

Outline

Diagnosis and Epidemiology

Differences between disorders

Treatment options
PSP History

Described in 1963

Progressive Supranuclear Palsy: A Heterogeneous Degeneration Involving the Brain Stem, Basal Ganglia and Cerebellum With Vertical Gaze and Pseudobulbar Palsy, Nuchal Dystonia and Dementia

John C. Steele, J. Clifford Richardson, Jerzy Olszewski

9 cases, 4 with detailed pathology

Progressive Supranuclear Palsy (PSP)

What is in a name?

- Progressive: belongs to neurodegenerative family like Alzheimer’s and Parkinson’s
- Supranuclear: the area of the brain that sends the initial signal to the nerve cells (of the eye muscles)
- Palsy: weakness or atrophy
- Steele-Richardson-Olszewski in 1963
PSP Epidemiology

Incidence: 5.3/100,000 over 50 (CBD not known)
Increases with age:
  • 1.7/100,000 in 50-59
  • 14.7/100,000 in 80-99
Often misdiagnosed, autopsy series
About 5% of patients in a Parkinson’s clinic
Cause: mostly unknown, FTDP, TDP-43, PGRN, CHMPB2, VCP

PSP Diagnosis

Gradually progressive disorder
Onset >40
Vertical gaze palsy
Prominent postural instability with falls in first year of onset
Corticobasal Degeneration (CBD or CBS)

Gradually progressive disorder

Asymmetric at onset (includes speech dyspraxia or dysphasia)

Presence of:

1. "Higher" cortical dysfunction (apraxia, cortical sensory loss, or alien limb)
   AND

2. Movement disorders (akinesia-rigidity, Levodopa resistant, limb dystonia or focal reflex myoclonus)
CBD Diagnosis

PSP and CBD Pathology

Tau Inclusions
More Alzheimer's like rather than Parkinson's
PSP Prognosis

Descriptive Epidemiology

<table>
<thead>
<tr>
<th></th>
<th>PSP</th>
<th>CBD</th>
<th>PD</th>
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<tbody>
<tr>
<td>Annual incidence / 100,000</td>
<td>1.1</td>
<td>&lt; 1</td>
<td>12</td>
</tr>
<tr>
<td>Prevalence / 100,000</td>
<td>5.6, 6.4</td>
<td>?</td>
<td>150-200</td>
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<tr>
<td>Mean onset age (sd)</td>
<td>63 (6.4)</td>
<td>63 (7.7)</td>
<td>59 (12.0)</td>
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<tr>
<td>Youngest-onset proven cases</td>
<td>Mid-40’s</td>
<td>Mid-40’s</td>
<td>Teens</td>
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<tr>
<td>Median survival</td>
<td>5.3, 5.9, 6.9, 9.7</td>
<td>7.9</td>
<td>9.4 (pre-levodopa)</td>
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<tr>
<td>% with positive family history in 1st-degree relatives</td>
<td>&lt;1%</td>
<td>+/- 0</td>
<td>20-25%</td>
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</tbody>
</table>
Eye

- **PSP**
  - Blurred vision
  - Double vision
  - Trouble walking down stairs, reading
  - Dry eyes
  - Blepharospasm

- **CBD**
  - Not really affected

- Treatment: Prisms, artificial tears, audio books, botulinum toxin

Speech

- **PSP**
  - Softening of the voice-parkinsonism
  - Spastic (choked quality)
  - Echoing

- **CBD**
  - Language problems - more AD-like
  - Halting
  - Stuttering
  - Slurring speech

- Treatment: Speech therapy, voice augmentation, alternate communication strategies
Swallow

- **PSP**
  - Trouble initiating swallow
  - Trouble with liquids first, then solids
  - Compulsive eating
  - Compulsive spitting
  - Drooling

- **CBD**
  - Late stage
  - Apraxia—trouble propelling food backwards

- Treatment: Speech therapy, thickeners, dietary modifications, feeding tube, anticholinergics

Posture

- **PSP**
  - Typically erect
  - Rigidity of neck and spinal muscles

- **CBD**
  - Not affected

- Treatment: Therapy, massage, botulinum toxin injection
Balance

- **PSP**
  - Non-specific dizziness common
  - Shuffling, freezing
  - Postural instability
  - Falls
  - Collapsing into chair

- **CBD**
  - More late stage

- Treatment: Therapy, early use of assistive devices

Cognition

**PSP**
- Frontal type dementia (different from AD)
  - Impulsivity
  - Perseveration
  - Apathy
  - Pseudobulbar affect
  - Impaired abstract thought
  - Decreased verbal fluency
  - Irritability

**CBD**
- Usually preserved
- Depression common as result
- Language deficits- expressive
- Apraxia of limb- loss of use of a limb
Dystonia

- PSP
  - Neck
  - Back
- Treatment
  - Botulinum toxin, anticholinergics (trihexyphenidyl)

- CBD
  - Limb

Mood/Personality

- PSP
  - Irritable
  - Impulsive
  - Depression
- CBD
  - Depression
**RD vs. PSP-P**  Williams et al *Brain* 2005

<table>
<thead>
<tr>
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<th>RD (n=56)</th>
<th>PSP-P (n=32)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Gender (male %)</td>
<td>64%</td>
<td>52%</td>
<td>NS</td>
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<tr>
<td>Age at onset</td>
<td>66 y</td>
<td>66 y</td>
<td>NS</td>
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<tr>
<td>Dysarthria</td>
<td>90%</td>
<td>56%</td>
<td>NS</td>
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<tr>
<td>Bradykinesia</td>
<td>98%</td>
<td>57%</td>
<td>NS</td>
</tr>
<tr>
<td>Rigidity</td>
<td>98%</td>
<td>57%</td>
<td>NS</td>
</tr>
<tr>
<td>Postural instability</td>
<td>100%</td>
<td>96%</td>
<td>NS</td>
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<tr>
<td>Limb dystonia</td>
<td>21%</td>
<td>42%</td>
<td>NS</td>
</tr>
<tr>
<td>Pyramidal sign</td>
<td>17%</td>
<td>16%</td>
<td>NS</td>
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<tr>
<td>LD-induced dyskinesia</td>
<td>2%</td>
<td>8%</td>
<td>NS</td>
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<tr>
<td>Age at death</td>
<td>72 y</td>
<td>78 y</td>
<td>0.041</td>
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<tr>
<td>Survival</td>
<td>54 y</td>
<td>81 y</td>
<td>&lt;0.001</td>
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<tr>
<td>Falls</td>
<td>100%</td>
<td>81%</td>
<td>0.001</td>
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<tr>
<td>Cognitive loss</td>
<td>87%</td>
<td>58%</td>
<td>&lt;0.001</td>
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<tr>
<td>Tremor</td>
<td>19%</td>
<td>44%</td>
<td>0.002</td>
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<tr>
<td>Extrapyramidal signs</td>
<td>100%</td>
<td>71%</td>
<td>&lt;0.001</td>
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<td>Visual symptoms</td>
<td>07%</td>
<td>04%</td>
<td>0.07</td>
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**Multiple system atrophy (MSA)**

**Criteria**

**Consensus criteria**

- **Definite:** histopathology (autopsy)
- **Probable:** autonomic criterion plus poorly levodopa responsive parkinsonism (or ataxia)
- **Possible:** poor levodopa responsive parkinsonism and one other feature from another system
Parkinsonism in MSA

- More symmetrical
- Poor levodopa responsiveness
- More problems with speech and airway
- Stridor

Cerebellar findings in MSA

- Gait unsteadiness (ataxia)
- Eye jerks (square wave jerks or nystagmus)
- Incoordination of limbs
Autonomic insufficiency with MSA

Problems regulating blood pressure
  “Neurogenic Orthostatic Hypotension”

Bowel
Bladder
Sexual dysfunction

Sleep in MSA

REM Sleep Disorder
Sleep apnea
Medications

Parkinson medication

- Used for parkinsonism: tremor, stiffness and slowness
- Levodopa most common (carbidopa/levodopa, Stalevo)
- Can try mirapex (pramipexole), requip (ropinirole) or Neupro (rotigotine)
- Amantadine
- Artane (trihexyphenidyl) or Cogentin (benztropine)

Medication

Drooling: Artane, Cogentin, Robinul, Atropine, botulinum toxin
Mood: SSRI (paroxetine, sertraline, citalopram)
Pseudobulbar affect: TCA (amitryptilline) or Nuedexta
Memory: Aricept/Exelon but may make mobility worse
Behavior:quetiapine, clozapine, maybe Nuplazid, mood stabilizers
Medication

Sleep problems: clonazepam, melatonin, sedating antidepressants
Posture and pain: botulinum toxin, gabapentin
Low BP: midodrine, fludrocortisone, droxidopa
Bladder medication
Bowel medication