Parkinson’s Disease

Tim Meagher, MB FRCP(C) FRCP(I)

Medical Director Munich Re, Canada
Medical Director ExamOne, Canada

AAIM Audio Seminar Series

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Parkinson’s Disease……200 yrs old and probably older

James Parkinson
(1755-1824)

Galen
175 AD
‘Shaking Palsy’

Mucuna pruriens

The original description 1817

1500 BC
‘Kampavata’

Pierre Roche Vigneron. (Paris: Lith de Gregoire et Deneux, ca. 1865)
Clinical Description of Parkinson’s Disease

- Tremor
- Rigidity
- Hypokinesia
- Postural instability
- Hypomimia
- Decreased blink rate
- Micrographia
- Stooped posture
- Shuffling gait

Charcot 1879

Nouvelle iconographie de la Salpêtrière, vol 1 (1888)

Clinical subtypes

- Tremor-dominant
- Akinetic-rigid
- Postural instability and gait difficulty

Tremor-dominant may have fewer neuropsychological symptoms and a better prognosis

Future course is difficult to predict
Non-motor symptoms

- Cognitive dysfunction and dementia
- Psychosis and hallucinations
- Depression, anxiety
- Sleep disturbances
- Fatigue
- Autonomic dysfunction
- Olfactory dysfunction
- Pain and sensory disturbances
Differential Diagnosis

- Essential tremor
- Dementia with Lewy bodies (DLB)
- Corticobasal degeneration
- Multiple system atrophy
- Progressive supranuclear palsy
- Idiopathic basal ganglia calcification
- Secondary parkinsonism
  - Drugs, toxins, head trauma (boxing), structural brain lesions, Wilson’s disease
  - Small vessel disease (Binswanger’s disease)
Parkinson’s Disease Dementia (PDD)

- 30% of PD patients have dementia (PDD)
- Is this a unique form of dementia, or is it
  - Alzheimer’s Dementia?
  - Vascular dementia?
  - Lewy Body dementia?
Etiology of Parkinson’s Disease: Lewy Body

- Intracytoplasmic
- Not limited to substantia nigra
- Stains + for alpha-synuclein
Pathophysiology of Parkinson’s Disease

- SN: substantia nigra
- Striatum: (caudate and putamen)
- GP: globus pallidus
- STN: subthalamic nucleus
- TH: thalamus
Understanding the Cause of Parkinson’s Disease

- Progressive brain involvement
- Asymptomatic phase
- Symptomatic phase

Braak, Cell Tissue Res 2004;318:121-134
PD Epidemiology

- 1 million people in North America
- Most common neurodegenerative disorder after Alzheimer’s dementia
  - Neurodegenerative disorders will cause more deaths than cancer in 2040
- Slightly more common in men
- Mean age at diagnosis age 70
- Rare before age 40
- Mortality is increased
- Morbidity is increased
  - Dementia a major issue
Risk factors for Parkinson’s Disease

- Age is most important risk factor
  - 0.3% in general population
  - 3% > 65 yrs
    - Number of cases is estimated to double in the next 20 years
- Smoking is protective
PD Dementia - risk factors

- Advancing age
- Number of years with PD
- Increasing severity of PD
Genetics of Parkinson’s Disease

- 20% of patients with sporadic PD have at least 1 affected first-degree relative
- First degree relatives are 2X more likely to develop PD
- Twin studies suggest that genetics important in early-onset PD
- 2000: first PD gene mutation described- PARK1 (SNCA gene)
- LRRK2, Parkin and PINK1, Glucocerebrosidase (GBA) gene mutations
Investigations

- No gold standard test
- Neuroimaging generally not helpful
  - Conventional MR usually performed to exclude other abnormalities
  - Clinical utility of PET, SPECT not yet established
Treatment of Parkinson’s Disease:

- Education
- Support
- Exercise
- Speech Therapy
- Medication
- Deep Brain Stimulation
Treatment of Parkinson’s Disease: Medication

- Levodopa
- Dopamine agonists
  - pramipexole
- MAO inhibitors
  - selegiline
- COMT inhibitors
  - entacapone
- Anticholinergics
- Amantadine
Treatment of Parkinson’s Disease: *Novel approaches*

- Neurotransplantation
- GDNF infusion
- Duodenal levodopa infusion
- Gene therapy
Treatment of Parkinson’s Disease: **Neuroprotection**

- 300-400,000 neurons produce dopamine
  - Can they be protected in some way?
Classifying the Severity of Parkinson’s Disease: Hoehn and Yahr Scale

1. Unilateral involvement only; usually with minimal or no functional disability
2. Bilateral or midline involvement without impairment of balance
3. Bilateral disease; mild to moderate disability with impaired postural reflexes; physically independent
4. Severely disabling disease; still able to walk or stand unassisted
5. Confinement to bed or wheelchair unless aided

Classifying the Severity of Parkinson’s Disease: Unified Parkinson Disease Rating Scale

1. Mentation, behaviour, mood (4 elements)
2. Activities of Daily Living (17 elements)
3. Motor (15 elements)
## PD: MR by Age Group

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<th>Age Group</th>
<th>Observed</th>
<th>Mortality Expected</th>
<th>MR (%)</th>
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<td>0.0521</td>
<td>0.0063</td>
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<td>45 - 49</td>
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<td>1.024</td>
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Mortality cancer risk in parkinsonian patients: A population-based study
With permission: F Sestier, Cours de médecine d’assurance, Université de Montréal
Thank You!