PARKINSON’S PRIMER
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DISCLOSURES

• None
PARKINSON’S DISEASE

- “Shaking Palsy” described by James Parkinson in 1817
- Prevalence is 1/100
- Most are over 60 years of age
- 1/15 are diagnosed under 50 years of age (early onset PD)
• Synucleiopathy
  • Abnormal protein, alpha-synuclein accumulates in neuron cell bodies
  • These form Lewy bodies pathologically

• In asymptomatic stage
  • Accumulate in the olfactory bulb, medulla and pontine tegmentum

• In symptomatic stage
  • Accumulate in the substantia nigra (par compacta), midbrain, and neocortex

• Final common pathway is decreased dopamine production
ETIOLOGY

- Unknown
- Genetic
  - 15% of PD patients have a first degree relative with PD
  - 3-5% have a gene mutation - not a single gene
- Environmental
  - Toxins, pesticides, MNDM
- Head trauma
  - Chronic Traumatic Encephalopathy and “punch drunk syndrome”
HISTORY

• Cardinal Motor Symptoms:
  • Tremor
  • Bradykinesia
  • Rigidity
  • Postural Instability
• Resting tremor
• May be mixed with some essential tremor
• Worse with stress
• Often fluctuates
BRADYKINESIA

- Slowing of movement
- Masking of face
- Hypophonic dysarthria
- Difficulty getting out of chair
RIGIDITY

• Overall rigidity
• Cogwheeling at wrists and ankles  
  • Micrographia  
  • Hand and leg stiffness  
• Axial rigidity  
  • Kyphosis  
  • Back pain
POSTURAL INSTABILITY

• Lack of balance
  • Small step size
  • Decreased arm swing
  • Pivot "en bloc"

• Falls
NON-MOTOR MANIFESTATIONS

• Mood changes
• Cognitive changes
• Autonomic dysfunction
• Sleep dysfunction
• Olfactory dysfunction
• Fatigue
• Pain
MOOD CHANGES

- Depression
- Anxiety
COGNITIVE CHANGES

- Memory impairment
- Language impairment
- Overall cognitive slowing
- Hallucinations/delusions
AUTONOMIC DYSFUNCTION

- Orthostatic hypotension
- Constipation and early satiety (weight loss)
- Urinary frequency
- Seborrhea dermatitis
- Excessive sweating (especially of the hands and feet)
SLEEP DYSFUNCTION

- REM sleep disorder
- Insomnia
- Excessive daytime sleepiness
- RLS/PLMD
OLFACTORY DYSFUNCTION

- Loss of smell years before onset of motor symptoms
  - Synucleinopathy of the frontal lobes/olfactory area
  - Testing “smell test” in clinical trials as a new cardinal sign of PD
• Clinical diagnosis
  • 4 cardinal motor signs
  • Non-motor signs
• Response to levodopa
• Rule out mimicking conditions
  • CT or MRI to r/o CTE, multiple stroke, NPH, Wilson’s disease
• MRI
  • Swallow tail sign
• Neurologists are approximately 80% accurate vs post mortem pathology
STAGES OF PARKINSON’S DISEASE

• First stage
  • Disability requiring pharmacologic treatment

• Second stage
  • Complications of treatment and advancing disease

• Third stage
  • Palliative treatment for numerous complications
TREATMENT OF PD

- Pharmacologic
  - Motor symptoms in early disease
  - Motor symptoms in later disease
  - Non-motor symptoms

- Non-pharmacologic
  - Exercise
  - Deep brain stimulation (DBS)
  - Experimental surgery
PHARMACOLOGIC TREATMENT OF EARLY MOTOR SYMPTOMS

• Levodopa
• Dopamine agonists
• MAO-B inhibitors
• Amantadine
• Anticholinergics (rarely used)

• NO SINGLE APPROACH BEST
• Dopamine can’t cross the blood brain barrier so levodopa is used with a decarboxylase inhibitor

• 2 preparations
  • Levodopa/carbidopa
  • Levodopa/benserazide

• Use early when motor function abnormality impairs quality of life
• Use lowest effective dose
• Give at regular dosing intervals
• Maximum of 5-6 doses a day is usually best
• Avoid slow release
DOPAMINE AGONISTS

• Second most potent class for motor symptom control

• 4 preparations
  • Ropinirole
  • Primipexole
  • Bromocriptine (rarely used)
  • Neupro (slow release patch) – rotigotine transdermal

• Likely cause less fluctuation in early disease

• Cause more side effects
  • Hallucinations, impulse control disorder, excessive daytime sleepiness, leg edema

• Use with caution, or not at all in patients over the age of 70
MAO-B INHIBITORS

- Prevent the breakdown of dopamine in the brain
- 2 preparations
  - Rasagiline
  - Selegiline
- May be used in early PD
AMANTADINE

- Likely multiple and poorly understood mechanism of action
- Rarely use as monotherapy
- Sometimes helps tremor
- Be careful in older patients
  - Hallucinations
  - Leg edema
  - Confusion
PHARMACOLOGIC TREATMENTS OF LATE MOTOR SYMPTOMS

• For the treatment of:
  • Fluctuation
  • Wearing off
  • Dyskinesias

• Add entacapone
  • COMT inhibitor which increases available dopamine
  • Reduce levadopa dose by 20% initially when adding

• Add rasagiline

• Each can decrease off time by 1.5 hours/day
TREATMENT OF NON-MOTOR SYMPTOMS

- Mood changes
  - Depression and anxiety
- Cognitive changes
  - Exelon
- Autonomic dysfunction
  - Orthostasis, constipation
- Sleep dysfunction
- Pain
  - Physiotherapy, analgesics, pregabalin
• Deep brain stimulation (DBS)
  • Used in advanced motor PD
  • Decreases off time and fluctuation by 50%
  • Decreases dyskinesias by 65%
  • Likely gives 5-10 years of effectiveness

• Stem cell transplantation
NON-PHARMACOLOGICAL TREATMENT

• Exercise
  • Reduces need for levodopa
  • Delays onset of levodopa complications
  • Dance, tai chi, treadmill, water exercise

• Physiotherapy
  • Gait re-training
  • Balance training

• Occupational therapy
  • ADL functional assessments lead to improved and safer independent living

• Social /psychological support
GOALS IN PARKINSON’S TREATMENT

- Maintain high quality of life for as long as possible
- Maintain independent living
- Support the patient and the caregiver
- Buy time for better pharmacologic and surgical treatments
KATHY’S APPROACH

• Early disease
  • Begin treatment when QOL is declining
  • Usually start with levodopa/carbidopa 100/25 tid or qid
  • Switch to levodopa/benserazide if not tolerated or I need a smaller dose
  • Use dopamine agonists only in younger patients (<60 yo)
  • Use rasagiline (Azilect) in early disease if not a clear need for levodopa
  • Use amantadine for severe tremor

• Mid disease (fluctuations)
  • Gradually increase levodopa to 5-6 doses/day
  • Then increase individual doses
  • Add entacapone – up to 6 doses daily
  • Consider adding rasagiline or a dopamine agonist
KATHY’S APPROACH – CON’T

• Late disease
  • Refer to movement disorder clinic for consideration of DBS
  • In older people, look carefully at QOL for patient and caregiver and consider safety
• Plus treat non-motor symptoms as they occur
• Encourage exercise at all stages of disease
MIMICKING CONDITIONS

- Drug induced Parkinsonism
- Parkinson Plus Syndromes
  - Lewy Body Disease (LBD)
  - Progressive Supranuclear Palsy (PSP)
  - Cortical Basal Degeneration (CBD)
  - Multiple System Atrophy (MSA)
PARKINSON’S PLUS SYNDROMES

• Early dementia
• Hallucinations/psychosis with low doses of levodopa
• Early falls/marked postural instability
• Ocular signs
• Pyramidal tract signs
• Early autonomic symptoms
• Symmetry of signs
• Truncal > appendicular rigidity
• Lack of resting tremor
LEWY BODY DISEASE

• Red Flags
  • Early dementia
  • Hallucinations/paranoia/delusions
  • Depression/anxiety
  • Psychosis/hallucinations with low dose dopamine therapy

• Treatment
  • Motor symptoms often improve with low dose dopamine
  • Use quetiapine or clozapine for psychiatric symptoms
  • Use cholinesterase inhibitors for dementia – rivastigmine, galantamine, donepezil
PROGRESSIVE SUPRANUCLEAR PALSY

• Tau protein disorder
• MRI – hummingbird sign

• Red flags
  • Lack of resting tremor
  • Severe postural instability and early falls
  • Axial rigidity more prominent than limb rigidity
  • Eye movement abnormalities – vertical, then horizontal

• Treatment
  • 1/3 of patients will have some response to levodopa
  • Supportive, physiotherapy, occupational therapy
CORTICAL BASAL DEGENERATION

- Frontoparietal cortical atrophy, plus basal ganglia and substantia nigra
- Tauopathy
- Red flags
  - Asymmetric rigidity in one arm
  - Alien arm/apraxia
  - Dystonic clenched fist
- Treatment
  - Try levodopa
  - Botox for rigid limb
  - Supportive
MULTIPLE SYSTEM ATROPHY

- Previously thought to be olivopontocerebellar degeneration, or striatonigral degeneration
- Most likely of the Parkinson Plus syndromes to be confused with idiopathic PD
- Red flags
  - Younger males (50’s)
  - Autonomic dysfunction
  - Cerebellar signs
  - Pyramidal signs (brisk reflexes, spasticity, upgoing toes)
  - MRI – hot cross bun sign
- Treatment
  - Treat autonomic dysfunction
  - Try levodopa
  - Supportive
DRUG INDUCED PARKINSONISM

- Caused by drugs that block dopamine
- Can be indistinguishable from idiopathic Parkinson’s Disease
  - Antipsychotic drugs (neuroleptics and atypical antipsychotics)
  - Gi drugs (motility drugs)
  - Calcium channel blockers, valproic acid, lithium
- Red flags
  - Use of offending drugs
  - Symmetric
- Treatment
  - Stop or switch offending drug
  - 10-50% will progress and need levodopa treatment (may have preclinical PD)
QUESTIONS?