Parkinson’s Disease

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First five years: Symptoms mainly motor

- Rigidity
- Tremor
- Bradykinesia
- Postural instability
PATHOLOGICAL FEATURES

Degeneration of pigmented Neurons
-Substantia nigra pars compacta

Lewy body formation

Motor
- Tremor
- Rigidity
- Bradykinesia

Non-motor
- Sensory
- Behavioral
- Memory
- Sleep fatigue
BRAAK STAGING FOR PD
NON MOTOR FEATURES OF PD

After five years: Non motor symptoms emerge

• Depression
• Apathy
• Anxiety
• Constipation
PATIENT 1

• 68 year old patient with Parkinson’s Disease (PD) diagnosed 4 years ago

• Wife reports more withdrawn, feeling sad and not interested in hobbies
IMPACT OF DEPRESSION

- Increased motor symptoms and disability
- Occurs independent of motor disability
- Increased caregiver burden and strain
- Worsening quality of life
- Increased risk of cognitive impairment/psychosis
• Maybe present several years prior to diagnosis of PD hence not just reactive to diagnosis

• Neurotransmitters involved: dopamine, serotonin, norepinephrine and acetylcholine
• Amitriptyline reported to be beneficial in evidence based review
• Caveat: anticholinergic side effects can worsen cognition and autonomic dysfunction
• Serotonin reuptake and norepinephrine serotonin reuptake inhibitors have been successful.
APATHY

- Reduced emotion
- Diminished motivation
- Lack of initiative
- Difficulty sustaining an activity
- Lack of concern
- Indifference
APATHY

• Present in 17-70% of PD patients

• Is not a simple reaction to disability

• Contributes to caregiver burden

• May fluctuate with motor function

• Testosterone deficiency may be present in some
ANXIETY

• Prevalence approaches 40%
• Often associated with depression
• May occur independently
• No correlation with disease severity
• May occur as an "off" phenomenon
• May culminate in panic attacks
After ten years: New non motor symptoms may emerge and may develop side effects of medications

- Hallucinations
- Short term memory problems
- Sialorrhea
- GI symptoms
• 69 year old gentleman with PD for 9 years. Onset with left leg tremor, shuffling gait, stooped posture

• Having formed hallucinations of a group of snipers firing at his home

• Has insight into the same but vivid nature is distressing
- Consider discontinuing anticholinergic medications
- Consider lowering total levodopa dose
- Atypical antipsychotics such as clozapine and seroquel might have a role
- Rivastigmine and Donepezil might help if associated with dementia
CASE VIGNETTE

- 72 year old patient with PD diagnosed 7 years ago
- Now having trouble with short term memory and multi tasking
- Has a tendency to get confused while driving to known locations
- Treatment: Consider donepezil/rivastigmine and driving evaluation
SIALORRHEA

• Socially embarrassing

• May cause aspiration

• Occurs due to decreased automatic swallowing resulting in pooling of saliva

• Flexed posture of neck may also impair swallow
• Sucking hard candy and chewing gum
• Anticholinergics can help but risk of memory problems and constipation
  • Atropine eye drops 1% 4 drops under the tongue every 4 hours
  • Botulinum toxin injections to salivary glands
• Mysticol clinical trial at Booth Gardner Parkinson’s center
GI SYMPTOMS

- 72 yr old gentleman with tremor dominant PD for 9 years
- Has been noticing increased drool, trouble swallowing
- Sometimes coughs and chokes on saliva
- Per wife has been restricting social activities due to same
DYSPHAGIA IN PD

- Secondary to rigidity and bradykinesia affecting bolus formation and transit
- May result in aspiration

Rx
- Speech/swallow therapy for swallowing techniques and changing food consistency
- Adjusting PD meds
- Rarely feeding tube
GASTROPARESIS

- Causes bloating, nausea and feeling of fullness

- Rx
  - Domperidone: available in Canada
  - Transdermal medications/duodopa pump helpful when absorption is affected
  - Apomorphine injections
GASTROPARESIS SYMPTOMS

- Reduced appetite
- Early satiety (fullness after a few bites)
- Nausea
- Vomiting (sometimes undigested food)
- "Heartburn" (gastroesophageal reflux)
- Abdominal bloating and distention
- Weight loss
TREATMENT OF GASTROPARESIS

- Prokinetic drugs
  - Dopamine antagonists
    - Domperidone - available in Canada
    - Do NOT use metoclopramide

- Frequent small meals
TREATMENT OF GASTROPARESIS

• Circumventing the stomach
  • Duodopa
  • Subcutaneous apomorphine
CONSTITUTION

- Secondary to prolonged transit time
- \( R_x \)
  - Increase fluid and fiber intake (20-35 grams of fiber/day)
  - Add stool softener
  - Consider lactulose/miralax, and enemas under M.D. supervision
- Defecation Difficulty
  - Undue straining and incomplete emptying
  - Keep stools soft, may try apomorphine before defecation
HYPERHIDROSIS

• Secondary to autonomic dysfunction in Parkinson’s disease
• Usually occurs during off periods though can occur in on state with dyskinesias
• \( R_x \)
  • Adjust dopaminergic medications based on off/on state hyperhidrosis
  • Non pharmacologic methods: sufficient hydration, avoid strenuous exercise, wear ventilated clothes
URINARY DYSFUNCTION

- Urinary frequency, urgency and nocturia
  - Oxybutynin: can cross into brain and cause confusion
  - Other options are:
    - Tolterodine, solifenacin and darifenacin

Clinical trial: MAESTRO

- Urinary Hesitancy:
  - Less common, rule out other conditions e.g., prostate enlargement
  - May need bethanechol or intermittent self-catheterization
76 year old gentleman with PD, onset 6 years prior with left hand tremor

Over the past few years increasing episodes of ‘violent dreams’ of chasing an intruder

Has acted it out once resulting in injury to wife
NON MOTOR FEATURES OF PD

After fifteen years:

• Memory problems
• Sleep disturbance
• Compulsive behaviour
REM Behavior Disorder
- Motor activity during REM with enactment of dream and loss of REM sleep muscle atonia
- May precede the diagnosis of PD by over 20 years
- Consider clonazepam or melatonin for treatment
SLEEP PROBLEMS

• Insomnia could be from:
  – Motor wearing off
  – Consider a long acting form of sinemet or dopamine agonist at night
  – Undiagnosed OSA: in 20-50% of pts with PD
  – Consider sleep study
REM SLEEP BEHAVIOR DISORDER

- May affect up to 50% of persons with PD
- Talking and shouting while asleep
- Intense, and sometimes violent, movements
- Involves "acting out" dreams
  - Ability to move while dreaming is retained
- May precede typical motor features of PD
REM SLEEP BEHAVIOR DISORDER: TREATMENT

• Safety and protective measures
• Eliminate potentially offending medications
  • Antidepressants
  • Cholinesterase inhibitors (e.g., donepezil, rivastigmine)
  • Beta blockers
  • Tramadol
  • Caffeine
• Melatonin
• Clonazepam
• Others (e.g., pramipexole, levodopa, gabapentin, clozapine)
CASE VIGNETTE

• 56 year old gentleman with PD onset 4 years prior with micrographia and right arm stiffness
• On pramipexole 1 mg tid with good motor response
• Wife has noted preoccupation with buying ‘toy helicopters’ and assembling same
• Spends hours at a stretch shopping online for same
ICD/DDS

• Spectrum of behavioral disorders
  • ICD (inability to resist impulses): gambling; shopping
  • RB (repetitive behaviors): punding; walkabouts
  • DDS (dopamine dysregulation): excessive dopaminergic med use resulting in disabling dyskinesias
ICD/DDS

- Risk factors:
  - Dopamine agonists > levodopa
  - Male sex, young age, long disease duration
  - History of substance abuse, novelty seeking personality traits
• Lower dopamine agonist dose/discontinue

• Switch between agonists

• Possible role for atypical antipsychotics
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Questions?