THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

# Case Studies in Movement Disorders

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## Disclosures



- Marissa Dean has nothing to disclose.
- Victor Sung has nothing to disclose.




## Objectives



- Recognize and describe phenomenology in common and uncommon movement disorders
- Be able to create a differential diagnosis for involuntary movements through case discussions
- Create a workup and treatment plan for movement disorders through case presentations

# Acknowledgments




- Patients and families for allowing the sharing of videos




# Case 1: Atypical parkinsonism

## Case 1



- 59 yo RH man with gait disorder/parkinsonism
- 3 years ago
  - Stumbling and shuffling
  - Drags left leg
  - Pain in left knee
  - 6 falls in past year (usually with bending, turning, or twisting)
  - Tends to drop pen out of left hand
  - Memory issues – forgetting appointments, details in conversation
  - Takes longer to process information (per brother)
  - Missed bill payments, overdrew account
- All symptoms have progressed over time

# Case 1



- Review of systems
  - No tremor, involuntary movements
  - No anosmia, change in taste
  - No change in voice, dysphagia
  - No constipation, dizziness
  - No dream enactment
  - Urinary issues for >12 years; urgency and incontinence; can't recall last time prostate was checked; no recent change
  - Independent in ADLs, driving (no issues)
  - Owns BBQ restaurant, but may need help with this now




# Case 1



- Medical history
  - Diabetes mellitus type 2, hypertension, OSA on CPAP
- Medications
  - HCTZ-Lisinopril, metformin
- Family history
  - Father diagnosed with NPH at ~65 yo. He had VPS, which made symptoms worse. He died 3 years (following a stroke) at 83 yo.
- Social history
  - Lives at home with 2 dogs. Drinks alcohol rarely (every ~6 months).




# Case 1– exam



- Eye movements – normal
- Muscle tone – normal
- Reflexes – grade 2 throughout with down going plantar response bilaterally
- Sensation – normal

# Case 1– video






# Case 1– group discussion

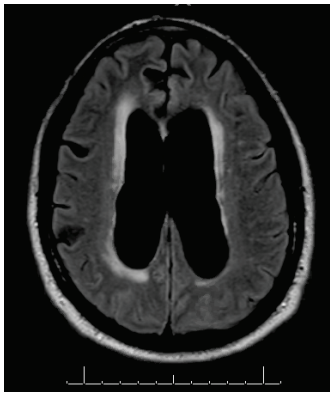


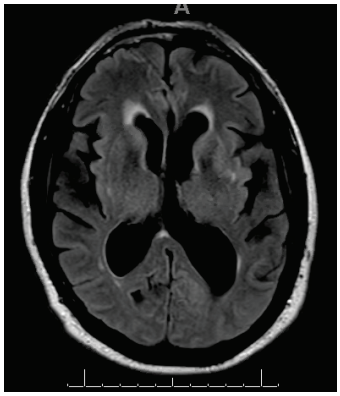
- What are the abnormal movements?
- Differential?
- Workup?




# Case 1– MR brain

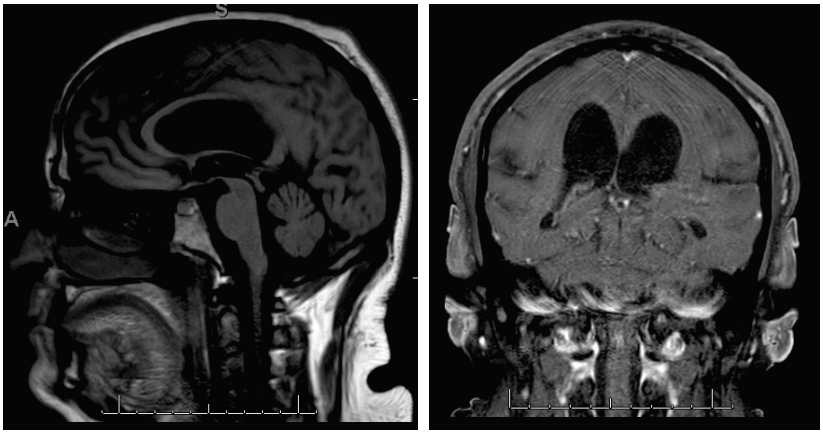






# Case 1– MR brain









# Case 1– lumbar puncture



- CSF
  - 56 protein
  - 2 WBC
  - 0 RBC
  - 80 glucose (98 serum)
- Timed 25-foot walk
  - Pre – 16.71 sec
  - Post (40 min) – 15.3 sec
  - Video




# Idiopathic Normal Pressure Hydrocephalus (NPH)



- What is it?
  - A syndrome? A neurodegenerative disease? Unknown?
  - Wet, wobbly, wacky
  - Water on the brain

  - 'Syndrome of gait dysfunction and enlarged cerebral ventricles in absence of another cause; frequently with cognitive deficits and bladder detrusor overactivity'
  - 'Generally, gait disorder + cognitive/urinary symptoms to make diagnosis'
  - 'Potential reversible cause of dementia'

Shprecher, Schwalb, Kurlan. Curr Neurol Neurosci Rep, 2008.

# NPH



- Gait disorder
  - 'Magnetic' – slow, decreased heel strike, wide base, postural instability
- Urinary incontinence
  - Detrusor overactivity
- Dementia
  - Psychomotor slowing, impaired attention, executive dysfunction, visuospatial dysfunction

Relkin, et al. Neurosurgery, 2005.




# NPH – diagnostic criteria



- Probable iNPH
  - >40 year old
  - Insidious progression over at least 3 months
  - CSF OP 70-245 mm H2O
  - MRI/CT with Evan's index at least 0.3
  - One of these: temporal horn enlargement, periventricular signal changes, periventricular edema, aqueduct/fourth ventricular flow void
  - Gait disorder – 2 abnormalities
  - Urinary or cognitive changes
  - No other suspected cause for hydrocephalus

Relkin, et al. Neurosurgery, 2005.




# NPH – imaging



- Which imaging marker is best?
  - Evan's index
  - Callosal angle
  - Compression of high-convexity sulci
  - Enlargement of Sylvian fissures
  - Presence of focally enlarged sulci
  - Width of temporal horns
  - Periventricular hyperintensities
- Recently published article comparing iNPH vs PSP vs MSA-P vs vasc dementia vs HC
  - Callosal angle <71 (>95% specificity, 69% sensitivity)
  - Evan's index >0.37 (>95% specificity, 58% sensitivity)
- **Our patient: Evan's index 0.32, callosal angle 56**

Fallmar, et al. Fluids Barriers CNS, 2021.

# NPH treatment



- CSF shunting
- High-volume LP (>30 mL) or lumbar drain helps predict likelihood of response to VPS
  - Sensitivity and specificity vary depending on study
  - Some patients will improve even more after VPS than was predicted after LP
- Unlikely to respond:
  - High white matter burden
  - Moderate to advanced dementia
- ~66% will have positive initial response to VPS; this drops to ~33% after 5 years
  - Within group of responders to CSF removal

Shprecher, Schwalb, Kurlan. Curr Neurol Neurosci Rep, 2008.
Relkin, et al. Neurosurgery, 2005.




# Case 1– video after VPS






# Case 1– take home points



- NPH is a potential treatable gait disorder
- Evan's index and callosal angle are radiological tools that assist in predicting positive response to VPS
- Some patients may improve even more after VPS
- Long-term benefits of VPS less clear

# Case 2: Atypical parkinsonism

## Case 2



- 69 yo RH man with gait disorder/parkinsonism
- 2 years ago
  - Initially, hesitations when walking
  - Now with freezing, more in the left foot than the right
  - One fall in past year – slipped on wet floor
  - Doesn't need assistive devices
  - Dysphagia – solids and liquids with choking episodes
    - Improved with lifestyle changes
- All symptoms have progressed over time
- Started on carbidopa-levodopa and pramipexole by Neurologist with improvement in walking
  - No wearing off, no dyskinesias




## Case 2



- Review of systems
  - No tremor, involuntary movements
  - Stiff when getting out of the car
  - No anosmia, change in taste
  - Voice is slurred, worse when tired
  - No constipation, urinary changes, dizziness
  - No dream enactment
  - No memory/cognitive changes
  - Independent in ADLs, driving (no issues)
  - No changes in mood/behavior

# Case 2



- Medical history
  - Pre-diabetes, hypertension
- Medications
  - Carbidopa-levodopa 25/100 mg TID
  - Pramipexole 0.5 mg TID
  - Doxazosin, lisinopril, metformin, pravastatin
- Family history
  - Strokes in mother and father. Father had shuffling gait. Mother had dementia.
- Social history
  - Lives at home with spouse. No alcohol, tobacco, illicit drug use.




# Case 2 – exam



- Muscle tone
  - Mild rigidity in upper extremities (L>R), left lower extremity, neck
- Reflexes
  - Grade 1in arms and patellar; absent at Achilles; downgoing plantar responses
- Sensation
  - Decreased vibration and temperature sensation in toes




# Case 2 – video

# Case 2 – group discussion

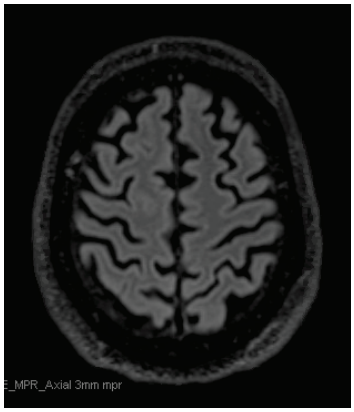


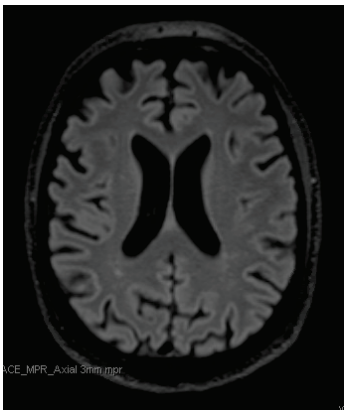
- What are the abnormal movements?
- Differential?
- Workup?




# Case 2 – MR brain





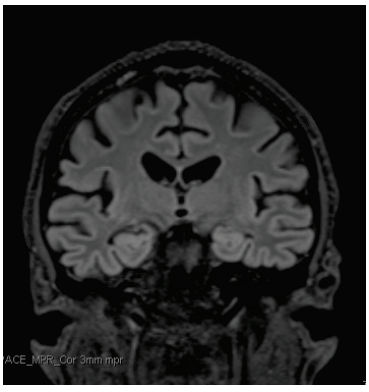



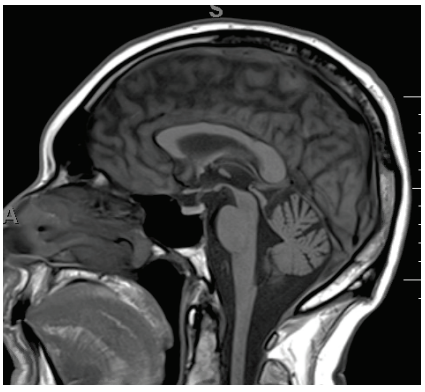




# Case 2 – MR brain





# Progressive Supranuclear Palsy (PSP)



- Neurodegenerative disorder
- Age >40 years, sporadic, gradual progression
- Definitive PSP – 4R-tau in neurofibrillary tangles, oligodendrocytic coils, astrocytic tufts
- Many clinical phenotypes:
  - Richardson's syndrome (PSP-RS)
  - Parkinsonism (PSP-P)
  - Progressive gait freezing (PSP-PGF)
  - Corticobasal syndrome (PSP-CBS)
  - Primary lateral sclerosis (PSP-PLS)
  - Cerebellar ataxia (PSP-C)
  - Speech/language disorders (PSP-SL)
  - Ocular motor dysfunction (PSP-OM)
  - Postural instability (PSP-PI)

Hoglinger, et al. Mov Disord, 2017.




# Progressive Supranuclear Palsy (PSP)



- Probable PSP
  - Vertical supranuclear gaze palsy or slow velocity of vertical saccades
  - Clinical syndrome
    - RS – >1 unprovoked fall or falls with pull test within 3 years
    - PGF – progressive gait freezing within 3 years
    - P
      - Akinetic-rigid parkinsonism (axial predom), levodopa-resistant OR
      - Parkinsonism plus: tremor and/or asymmetry and/or levodopa-responsive
    - F – 3 of the following are persistent
      - Apathy, bradyphrenia, dysexecutive syndrome, reduced phonemic verbal fluency, impulsivity/disinhibition/perseveration,

Hoglinger, et al. Mov Disord, 2017.




# Progressive Supranuclear Palsy (PSP)



- Possible and suggestive criteria also proposed
- Clinical clues may help
  - Levodopa-resistance
  - Hypokinetic, spastic dysarthria
  - Dysphagia
  - Photophobia
  - Predominant midbrain atrophy or hypometabolism

Hoglinger, et al. Mov Disord, 2017.

# Imaging in PSP

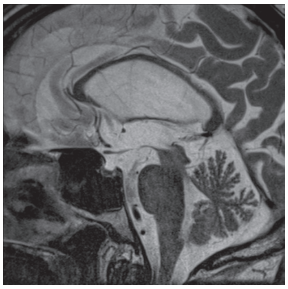


- Midbrain to pons (base) ratio
  - Midbrain about 2/3 the size of pons normally
  - If midbrain ½ size of pons (or smaller), suggestive of PSP
- Hummingbird (penguin) sign
  - Flattening of superior aspect of midbrain
- Mickey mouse appearance or morning glory sign

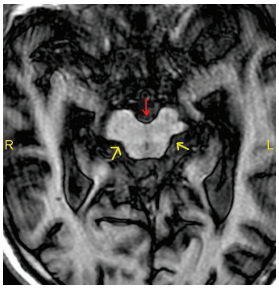



# Imaging in PSP





Hummingbird/penguin




Mickey mouse/morning glory

https://radiopaedia.org/articles/progressive-supranuclear-palsy-1




# Case 2 – take home points



- Early PSP may not have a palsy, but instead slowing of vertical saccades
- There are many described phenotypes in PSP
- 4R-Tauopathies is being used more in the literature to combine all phenotypes into one entity

# Case 3: Abnormal facial movements

## Case 3



- 89 yo RH woman with difficulty with balance and coughing
- 15 months ago, shortly after husband died
  - Wide-based walking and off balance
  - Coughing
  - Went to ED – told it was a side effect from Zoloft, and this was stopped
    - Had been taking Zoloft for past 8 years for depression
  - Then, all symptoms worsened
  - Diagnosed with PD, started on C/L, caused emesis, stopped
- Within past year
  - Now with facial grimacing and blinking
  - Sensation of something in between her throat and nose, and this makes her cough
  - No relief with cough, unable to suppress
- Presented to ED due to frequent coughing causing respiratory distress and fatigue




## Case 3



- Medical history
  - Stroke (unknown symptoms), hypertension, depression
- Medications
  - ASA, docusate-senna, loratadine, montelukast, omeprazole, sertraline 25 mg, tizanidine 2 mg BID, trazodone 100 mg QHS
- Family history
  - Depression in son.
- Social history
  - No alcohol, tobacco, illicit drug use.

# Case 3 – exam



- Eye movements – normal
- Muscle tone – normal
- Reflexes
  - Grade 3 in arms and absent in legs; downgoing plantar responses
- Sensation – normal
- Gait – slow and cautious




# Case 3 – video






# Case 3 – group discussion



- What are the abnormal movements?
- Differential?
- Workup?
- Treatment?

# Case 3 – 1 month follow up



- Started on clonazepam 0.25 mg BID in hospital
  - Improvement of facial movements
  - Some wearing off in middle of the day
- Suspected tardive dyskinesias (?exposure from hospitalization one year ago)
- Plan: increase clonazepam up to 0.5 mg BID
  - If no improvement, will start deutetrabenazine




# Case 3 – hospital records



- Patient reported receiving botulinum toxin injections for jaw clenching in the past
- Perphenazine listed as discharge med
  - *C/L 25/100 mg TID given during hospitalization with improvement of gait (but also on perphenazine at the time)
  - Possible drug-induced parkinsonism that resolved after stopping perphenazine




# Case 3 – 8 month follow up



- Started on deutetrabenazine in between visits and on 12 mg BID
- Weaned off clonazepam
- Video

# Tardive dyskinesia – DSM-5



- Involuntary athetoid or choreiform movements generally of the tongue, lower face and jaw, and extremities developing in association with a neuroleptic medication.
  - Movements for >4 weeks
  - Exposure for >3 months
- However, may develop after shorter timeframe in older people
  - Also with medication cessation, lowering/increasing dose
  - Symptoms >8 weeks also considered tardive
- **Tardive dystonia and tardive akathisia considered separate diagnoses, but may occur together




# Tardive dyskinesia



- Buccal-orolingual stereotypy is commonly seen
- 30% of people on antipsychotic meds
- Long term risk
  - 25% at 5 yrs
  - 49% at 10 yrs
  - 68% at 25 yrs
- Risk factors
  - Increased age, female, more portent DRBAs (D2 receptor), dose, exposure duration

Acquino and Lang. Parkinsonism Rel Disord 2014
Lerner et al. Psychiatr Clin Neurosci 2015




# Tardive dyskinesia – treatment



- VMAT2 inhibitors – 2 are FDA approved for treatment of TD
  - Deutetrabenazine
    - More dose ranges, but complicated titration schedule form 6 mg BID up to 24 mg BID
  - Valbenazine
    - Only 2 dose options, but easier to administer (daily dosing)

# Case 3 – take home points



- With stereotyped chorea-like movements, always consider TD, even if the exposure is not known at the time
- TD can develop more acutely in the elderly population
- Two FDA-approved treatments for TD