



# Neurology Cases

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## Overview

- Normal Pressure Hydrocephalus
- Lewy Body Dementia
- Parkinson's Disease

## Case 1: Clinical History

- 69y/o man presents for a 2<sup>nd</sup> opinion regarding his diagnosis of AD. More forgetful past 1 year. Wife says- more withdrawn and irritable.
- Saw neurologist ~ 1 yr ago and had a 'nuclear medicine study that showed Alzheimer's disease.' Started on Aricept.
- In past 6 months more withdrawn/less active. Increased # of falls. Stopped reading (used to be avid reader). Wife says he is depressed.

## History:

- Med Hx: Chronic renal insufficiency, HTN, DM II, Diabetic peripheral neuropathy, osteoarthritis, obesity.
- Surg Hx: Pacemaker, Cataract surgery bilateral. Tonsillectomy
- Social Hx: Education level – Masters in Teaching. Distant tobacco use. Occasional wine with dinner. No regular exercise.
- Family Hx: Father died 85y/o- Alzheimers. Mom died 79y/o- DM, CAD-MI.

Allergies: NKDA

## Medications

- Aspirin
- Citalopram
- Aricept
- Enablex
- Pravastatin
- Diovan
- Lasix
- Clonidine
- Amlodipine
- Toprol XL
- Terazosin
- Prandin
- Glipzide
- Tylenol Arthritis
- Hydrocodone/APAP
- MVI
- Vitamin C
- Vitamin B complex
- Fish oil

## Neuro Exam

- Vitals: Ht: 6ft. Wt: 265 lbs. BP 130/78 HR 82.
- MS: Alert/O to full date. Fluent speech, no dysarthria or aphasia. Mildly flattened affect. MMSE 30/30. 28 animals in 1 minute. Lists Presidents. Clock drawing correct.
- CNs: normal.
- Motor: normal muscle tone/bulk. Strength 5/5 throughout, no resting tremor.
- Sensory: decreased pin/lt over toes to ankles, Vibration decreased in toes, Proprioception intact.
- Reflexes: diminished throughout/ absent at ankles.
- Cerebellar: No dysmetria, FNF, RAM, H-S. Romberg negative.
- Gait: mildly widened stance. Uses a cane but can walk without it although appears unsteady. No shuffling.

## Assessment

- Requesting 2nd opinion re: dx of Alzheimer's disease
  - 30/30 on MMSE..
  - Depression/Pseudo-dementia
- Possible normal pressure hydrocephalus (NPH).
  - Head CT needed.
- Depression –
  - Taking Citalopram
  - Request records

## Record Review

- One year ago difficulty with memory and gait. CT head showed enlarged ventricles.
- CSF Cisternogram - negative.
- Diagnosed with AD- started on Aricept.
- Falls- blamed on peripheral neuropathy
- Urinary incontinence -blamed on 'getting older'.

## Record Review (continued)

- Depression- tried Zoloft, Paxil, Citalopram.
- Neurologist not convinced AD; suspected pseudodementia

## Follow up

- Reviewed records with patient – questioned AD diagnosis.
- Despite the negative CSF Cisternogram can still have NPH.
  - CT head.
- Depression – tried 3 SSRIs. Started SNRI. Weaned Citalopram and started him on Venlafaxine 37.5mg x 2 weeks then increase to 75mg/day.

## Results

- Head CT – compared to prior scan 1 yr earlier there it stable diffuse ventriculomegaly. Stable mild chronic microvascular ischemic changes. Stable mild generalized volume loss.
- Labs: CMP/CBC/TSH/Vit B12 all normal except Glucose elevated and renal function mildly impaired.

## NEXT STEP

- Sent patient for large volume spinal tap with pre and post Tinetti scale.
- Balance section: Pre 5/16 ..... Post 11/16
- Gait section: Pre 3/16..... Post 7/16
- Overall: Pre 8/16 ..... Post 18/28

## Neurosurgery Referral

- Neurosurgeon reviewed records documenting subjective and objective improvement in gait/balance.
  - self report of less urinary urgency
  - felt like he could concentrate better when reading.
- Ventriculoperitoneal Shunt placed

## 1 Month Post VP Shunt

- Urinary incontinence resolved almost immediately. Reported headache (next slide)
- Gait improving – outpatient PT. No falls since spinal tap.
- Cognition –thinking more clearly and informed me he had stopped Aricept 3weeks after shunt placement
- Depression - Venlafaxine 75mg twice daily and was 'better'. Less irritable, more outgoing. More motivation to do things. Resumed reading.



## Headache

- Reported headaches since shunt placement- whole head pressure/ache. 5-6/wk . Relieved temporarily with Tylenol arthritis 650mg x 2 pills. Some photophobia, no n/v or vision changes.
- Returned to neurosurgeon for shunt flow adjustment and h/a resolved.

## 4 months post shunt

- Gait – playing golf again
- No urine incontinence- stopped Enablex
- Memory – remains off Aricept, thinking clearly. MMSE 30/30
- Depression- felt like “life back”. Instructions to wean off Venlafaxine



## 1 year post shunt

- Patient and family remark on his improved quality of life.

## Normal Pressure Hydrocephalus

- Triad of gait disturbance, urinary incontinence, and a dementing process
- CT/MRI: ventricular enlargement disproportionate to cortical atrophy and small-vessel ischemic changes
- Confirmed by beneficial response to large-volume cerebrospinal fluid drainage (30-50 ml)

## Differential Diagnosis for NPH

- Vascular dementia – Asymmetric findings on exam (Babinski sign, hyperreflexia, spasticity).
  - Both NPH and VaD with executive dysfunction but frontal lobe features (apathy, abulia) suggest NPH.
- Dementia with Lewy Bodies (DLB) or Parkinson disease dementia – cognitive dysfunction more prominent psychotic features, visual halluc.
- Alzheimers disease – AD does not impair gait early in disease course but older pts have gait dysfunction from other things (arthritis, spondylosis, vestibular dysfxn, visual impairment, neuropathy, etc). Presence of cortical features (aphasia, apraxia) more likely to support AD

## Normal Pressure Hydrocephalus

- Surgical treatment by CSF shunting procedure
- Good prognosis is associated with presence of full triad, short duration of symptoms, mild dementia, lack of significant cerebral atrophy
- Complications: shunt malfunction, headache, subdural hematoma, infection, seizure

## Case #2: Clinical History

- 72y/o man -2<sup>nd</sup> opinion, confusion.
- 11/2014- surgery for Achilles Tendon rupture. Post-op confusion/hallucinations. Inpatient rehab.
- 1/2015- wound infection requiring PICC line for IV Rocephin and then 'other antibiotics.' Became more confused.
- Neurology eval - MRI brain and EEG and dx with "metabolic encephalopathy."

## History- cont'd

- PCP treated with "IV Detox".
  - gradually less confused over next few months.
  - Overall took 9 months to heal.
  - 8/2015 driving again but wife not confident in that skill.
- 10/2015- started 'slowing down' in his movements and seemed depressed.
- Inpatient psychiatric admission.
  - Discharged on Temazepam 15mg qhs. Wife reports he tried many medications but they made him "out of it" and "made him drool."

## History-cont'd

- Alprazolam for agitation = increased confusion.
- History of vivid dreams/acting out dreams -now more frequent.
- Recently trouble getting going, getting in/out vehicle, turning over in bed.

## History cont'd

- PMHx: HTN, depression, osteopenia, MCI, Cervicalgia
- PSHx: Achilles tendon rupture repair 11/2014
- SocHx: Married, No tobacco or alcohol. Occupation: retired manual labor. Education level: high school
- FamHx: Father died 80y/o –MI. Mom is 93y/o-has AD. 3 Children -healthy

## Medications

- Current: Lisinopril 20mg, Tamsulosin 0.4mg, Coconut oil 1 Tbs, Omega 3 fish oil, B-complex, Vit D 1000U
- Meds Tried: - Lorazepam 1 mg, alprazolam 0.25 mg, temazepam 15 mg, Quetiapine 25 mg, Depakote ER 500 mg, Risperidone .25 mg

## Exam

- Vitals: Ht 6'1', Wt 155lb, BP 126/68 HR 84
- General: Cooperative, doesn't offer spontaneous conversation. Wife answers for him.
- Heart- regular, no murmurs. Lungs: Clear in all fields.
- Neuro: MS- Alert, Oriented to all aspects of date EXCEPT year, MOCA 10/30, SLUMS 14/30. Names only 4 animals in 1 minute. Unable to draw clock correctly.

## Exam -cont'd

- CNs, Sensory, Reflexes, Cerebellar: all normal
- Motor: slightly increased tone in upper extremities. No resting or intention tremor. Finger and heel tapping slow b/l. RAM slow b/l.
- Gait: unsteady on feet with trouble rising from chair unless uses arms. Narrow based, small steps. Unable to walk on heels, toes, or in tandem. Romberg negative.

## Imaging/Labs

- Brain MRI with and without contrast 12/18/15-stable appearing brain MRI compared to May 2015. Mild atrophy. No significant microvascular ischemic disease. No mass, hemorrhage, or infarct.
- Labs: CMP, CBC, TSH all normal. Vitamin B12 1185

## Assessment/Plan

- Constellation of symptoms: parkinsonism, hypersensitivity to medications, REM sleep behavior disorder, fluctuating confusion with visual hallucinations and delusions.
- Symptoms c/w Dementia with Lewy bodies (DLB).
- Cerebral PET scan ordered

## Results

- Cerebral PET scan 1/27/16- statistically significant profound cerebral hypometabolism involving L>R cerebral hemisphere's. Presence of occipital lobe hypometabolism suggestive of DLB.



## Treatment of Case #2

- Hired help
- Donepezil 5mg→10mg
- Quetiapine 25mg →50mg.
- Sinemet 25/100. 3x/day -increased hallucinations.

## Dementia with Lewy Bodies

### Clinical Features

- Second most common form of degenerative dementia in old age
- Early psychotic symptoms: hallucinations/ delusions
- Mild extrapyramidal dysfunction
- Fluctuations in attention or level of arousal
- Orthostatic hypotension, syncope
- Depression
- Diurnal variations in behavior
- Neuroleptic sensitivity
- REM sleep behavior disorder

## Dementia with Lewy Bodies

### Pharmacological Management

DLB patients DO have cholinergic deficits. Multiple anecdotal reports, open label studies, and limited # of RCT suggest cholinesterase inhibitors are helpful in DLB. Reported benefits in cognition, behavior fluctuations, psychotic sx

- Cholinesterase inhibitors: Rivastigmine, Donepezil
  - No worsening of motor function
  - Improvement of total Neuropsychiatric Inventory (NPI) score
  - Improvement of 4-item (delusion, hallucination, apathy, depression) subscore

## Neuropsychiatric Inventory Domains

- Delusions (paranoia)
- Hallucinations
- Agitation / aggression
- Dysphoria
- Anxiety
- Apathy
- Irritability
- Euphoria
- Disinhibition
- Aberrant motor behavior
- Nighttime behavior disturbance
- Appetite/ eating abnormalities

## Dementia with Lewy Bodies

### Pharmacological Management (cont)

#### Antipsychotic agents:

- Neuroleptic sensitivity to typical antipsychotics
- Low dose atypical antipsychotics are tolerated.
- Nuplazid (Pimavanserin)

#### Dopaminergic therapy:

- Carbidopa/levodopa- watch for orthostatic hypotension

## Case 3: Clinical History

- Mr. M is a 57y/o RH man who presents for 2<sup>nd</sup> opinion regarding diagnosis of essential tremor.
- He reports onset of tremor in his hands with activity about 1.5 yrs ago. Initially only when turning pages while reading then also when using tools in his workshop. Denies resting tremor.
- He was started on Propranolol 60mg/day for tremor and became hypotensive. Then switched to Primidone 50mg qhs which he is currently taking and has never been convinced it helps. He did not return to neurologist so his PCP has been prescribing the Primidone .
- PCP ordered MRI Brain prior to visit – it is unremarkable.

## Case 3: history cont'd

- Wife reports that when he washes the car he “shuffles like an old man”. Also she doesn’t like his new “habit” of pursing his lips and sucking on the end of his tongue. She says he gets annoyed with her for asking him if he is upset because “he looks it” to her. He gets annoyed with her for telling him to “speak up” as she says “he mumbles.”
- Denies trouble initiating movement but sometimes will shuffle feet and take small steps. Says he feels ‘weak.’ Handwriting is smaller and sloppier. Sometimes has trouble getting out of a car and turning over in bed. +hypophonia (per wife, pt denies). No anosmia, no constipation.

## History cont'd

- Med Hx: Hyperlipidemia, HTN, restless leg syndrome, OSA, anxiety
  - Surg Hx: b/l knee arthroscopic surgeries
  - Social Hx: Married, no children. Occupation: accountant (just retired). No tobacco or etoh. Drinks “red bull” for energy daily.
  - Family Hx: Mom died 76y/o Bladder CA. Dad died 80y/o CHF, stroke. Dad had tremor- undiagnosed type. Brother 50y/o healthy.
  - Meds: Simvastatin 20mg, Lisinopril 10mg, Paroxetine 20mg, Primidone 50mg qhs
  - Allergies: NKDA
- ROS: see HPI, +RLS occurring “most nights” ~7pm

## Physical Exam

- Vitals: Ht 5'9", Wt 160lbs BP 128/78 HR 78
- GENERAL: Pleasant cooperative, NAD.
- HEENT: NC/AT sclera anicteric. Seborrheic dermatitis present in perioral area. NECK: supple. EXTREMITIES: no edema or skin lesions.
- Heart: regular, no murmurs. Lungs: Clear in all lung fields.
- **NEURO:** MENTAL STATUS: alert and attentive, oriented to full date. Speech is fluent. No dysarthria or aphasia. MOCA 28/30 (missed 2 points serial 7 subtraction). Trails B took 1:20 (nl ≤ 1:30).
- CNs: PERRL, EOMI, no nystagmus. FVF to confrontation. No facial asymmetry to sensory or motor testing. Facial expression does not appear diminished to this examiner. Hearing intact to finger rub b/l. Palate elevates symmetrically. Tongue is without atrophy and protrudes midline

## Exam cont'd

- MOTOR: Normal muscle bulk/tone, no drift. No cogwheel rigidity. Strength 5/5 bilateral UE/LEs. Subtle resting tremor right 5<sup>th</sup> digit. With FNF there is slight endpoint tremor b/l. Fist open/close subjectively feels the same but objectively less smooth on right. Finger tapping bradykinetic with low amplitude on R, nl on left; heel tapping less smooth on right (per examiner).
- SENSORY: Intact to light touch, pinprick, vibration, proprioception.
- REFLEXES: Symmetric: 2 UEs and patellar, 1 Achilles b/l. No clonus. Plantar reflex is flexor bilaterally.
- CEREBELLAR: FNF, RAM, H-S without dysmetria/ataxia.
- GAIT: Arises from chair w/o using arms. Normal stride length, decreased arm swing on right, no tremor with walking. Able to walk on heels, toes and tandem. Romberg negative. No retropulsion.

## Impression

- Parkinsonism – probably idiopathic Parkinson's. Evidence to support diagnosis include asymmetric motor findings on exam with resting tremor and the clinical history of PD features (shuffling, micrographia, trouble initiating mvt, decreased facial expression and hypophonia).

## PLAN

- Advised patient I wanted to review MRI Brain
- Requested labs from PCP to confirm no gross metabolic abnormalities – normal CMP, Thyroid function. Pt denied any exposures to pesticides or other toxic substances (future slide).
- Discontinue Primidone
- F/up 1 week



## Plan -cont'd

- At f/up, pt says no worse without the Primidone
- Educated him on medications used to treat symptoms of PD
  - No proven neuroprotective or disease modifying therapy exists
- Start trial of Ropinirole for both RLS and PD sx's. 0.25mg TID x 1 wk. If no adverse SEs and no improvement in sx's then increase to 0.5mg TID x 1wk. Educated to increase 0.25mg TID each week up to 4 pills (1mg) TID
- F/up 4 weeks

## Follow up

- Pt taking Ropinirole 0.75 TID and pleased with results.
- Reports resolution of RLS symptoms, moving more easily, feels 'stronger', and isn't noticing the tremor in right hand anymore other than when tired.
- Wife says he moves 'a little faster' and she hasn't noticed the shuffling. She still sees him purse his lips but less often. He still doesn't talk loud enough and he says, "she needs hearing aids."



## PD Cardinal Motor Features

- **Bradykinesia** – slowness of movement and small movements. Reduced blinking, face expression and gesturing. Hypophonia, micrographia, ↓ arm swing, start hesitation, shuffling steps, freezing
- **Tremor**: (usually resting) “pill-rolling,” often involves thumb.
- **Postural Instability**: retropulsion on pull test. Falls, stooped, flexed posture.
- **Rigidity**- resistance to passive manipulation that is NOT velocity or direction dependent (unlike spasticity)

## PD Non-Motor Features

- REM behavior disorder, daytime sleepiness
- Anosmia
- Autonomic dysfunction
- Depression and anxiety
- Fatigue
- Pain and sensory symptoms
- Cognitive impairment and dementia

## Drug Overview for PD

- L-Dopa (with carbidopa) – most effective and usually best tolerated. Improves bradykinesia, rigidity, tremor and gait. By mid-late disease almost always needed. COMT Inhibitors improve bioavailability and duration of effect.
- DA agonists (ropinirole, pramipexole, rotigotine, apomorphine) –in young patients, less prone than l-dopa to causing dyskinesias. More prone to hallucinations/nausea.
  - Sleep attacks (can be abrupt and cause car crashes)
  - Orthostasis, leg edema
  - Compulsive behaviors

## Drug Overview for PD (cont'd)

- Anticholinergics (trihexyphenidyl, benztropine) can help with tremor and rigidity
- MAO-B Inhibitors (selegiline, rasagiline)
- Amantadine- helps with tremor and sometimes dyskinesias

## Functional Neurosurgery in PD

- Lesioning
  - Thalamotomy
  - Pallidotomy
- Deep Brain Stimulation
  - Thalamic DBS
  - Pallidal DBS
  - Subthalamic DBS

## DBS: Who Benefits and How?

- Not Neuroprotective
- For motor fluctuations and dyskinesias refractory to medical management
- Prolongs the best dyskinesia-free ON state that can be obtained on meds alone.
- Contraindications: Severe psychiatric disease, cognitive impairment, postural instability and falls (DBS could worsen these)
- Patients do better for some years but eventually continue to decline.

