Presenting history

- 68M referred to KCHC clinic for blurry vision
- No other ocular or visual complaints
- No past ocular history
- ROS: no flashes, floaters, curtains, diplopia, ophthalmoplegia
Presenting history (cont.)

• PMH: Parkinson’s disease, DM2
• Meds: sinemet
• All: nkda
• FH: no known glaucoma or blindness
• SH: no tob, etoh, illicit drugs; Indian American origin
Exam

• General: wheelchair bound, severe rigidity and bradykinesia when transferring to slit lamp chair
• BCVA: 20/70, 20/50
• Pupil: 3-2 ou, no rapd
• EOM: see video
• CVF: full ou
• Ta: 10/11
Slit lamp

- **SLE**
  - L/l: wnl ou
  - C/s: tr inj ou, conjunctivochalasis ou, nasal pterygium od
  - K: severe spk ou
  - Ac: d/q ou
  - Iris: r/r ou
  - Lens: ns ou

- **DFE**
  - Vit: clear ou
  - ON: 0.55 s/p ou
  - Macula: flat ou
  - Vessels: wnl ou
  - Periphery: wnl ou
Patient care
Recap

• Almost absent vertical saccades and smooth pursuit
• Hypometric horizontal saccades
• VOR essentially intact
Types of eye movement

• Gaze Stabilization
  – Vestibulo-ocular
  – Optokinetic

• Gaze shifting
  – Vergence
  – Smooth Pursuit
  – Saccade
Neural motor centers for saccades

- **Vertical**
  - EBN in rostral interstitial nucleus (rostral iMLF)

- **Horizontal**
  - EBN in paramedian pontine reticular formation (PPRF)

- Cortex controls saccades via superior colliculus

http://cueflash.com/decks/CONTROL_OF_EYE_MOVEMENTS_-_57
Recap

- Almost absent vertical saccades and smooth pursuit
- Hypometric horizontal saccades
- VOR essentially intact
Differential diagnosis

• Progressive supranuclear palsy
• Acquired ocular motor apraxia
• Corticobasal degeneration
• Multiple system atrophy
• Idiopathic Parkinson’s disease
Impression:
68M h/o previously diagnosed Parkinson’s disease presenting to eye clinic with vertical gaze palsy thought to be 2/2 progressive supranuclear palsy (PSP).

Plan:
Discussion of:
• Clinical features of PSP
• Current diagnostic criteria as well as potential future modalities to assist in the diagnosis
• Clues to distinguish PSP from closely related diseases
PROGRESSIVE SUPRANUCLEAR PALSY
Progressive supranuclear palsy (PSP)

- Rare neurodegenerative disorder characterized by motor and ocular symptoms
- J. Clifford Richardson first presented 8 cases in 1963 at ANA
- Richardson and John Steele authored the first paper the following year along with pathologist J. Olszewski
  - Richardson-Steele-Olszewski Syndrome

Medical knowledge
Epidemiology

• Incidence $\rightarrow \sim 1.5/100,000$

• Average age of onset $\rightarrow 65$

• Slight male predominance

• Median survival $\rightarrow 6-7$ yrs from onset
  – Death usually from aspiration pneumonia or other infections related to immobility or from consequences of postural instability (ie. falls)
NINDS-SPSP diagnostic criteria

- Possible PSP
- Probable PSP
- Definite PSP
Possible PSP

- Gradually progressive disorder
- Onset age $\geq 40$ years
- No evidence of other disease explanation
- Either vertical supranuclear palsy

OR

Both slowing of vertical saccades and prominent postural instability with falls in the first year of onset
Probable PSP

• Gradually progressive disorder
• Onset age >= 40 years
• No evidence of other disease explanation
• Vertical supranuclear palsy

AND

Prominent postural instability with falls in the first year of onset
Definite PSP

- Possible PSP or Probable PSP
  
  AND

  Histopathology typical of PSP
Supportive clinical features

• Symmetric akinesia or rigidity
• Abnormal neck posture
• Poor response to levodopa
• Early dysphagia and dysarthria
• Early cognitive impairment with at least two of:
  – Apathy
  – Impaired abstract thought
  – Decreased fluency
  – Frontal release signs
Exclusion criteria

• Recent history of encephalitis

• Alien limb syndrome, cortical sensory deficits, focal frontal atrophy

• Hallucinations or delusions unrelated to dopamine therapy

• Cortical dementia of Alzheimer type

• Prominent early cerebellar symptoms or unexplained dysautonomia
Exclusion criteria (cont.)

- Severe asymmetric parkinsonian signs
- Neuroradiologic evidence of relevant structural abnormalities
- Whipple’s disease confirmed by PCR
Oculomotor abnormalities

• Early stages
  • Slowness of vertical saccadic movements
  • Hypometric horizontal saccades
  • Reduced blinking
  • Square wave jerks

• Middle stages

• Late stages
Oculomotor abnormalities

- Early stages

- Middle stages
  - Supranuclear vertical gaze palsy
  - Lid retraction with rare blinking
  - Impaired convergence
  - Apraxia of eyelid opening or closing

- Late stages
Oculomotor abnormalities

- **Early stages**

- **Middle stages**

- **Late stages**
  - Supranuclear horizontal gaze palsy
  - Loss of oculocephalic reflexes
  - Blepharospasm
  - Disconjugate gaze
Clinical variants

• Richardson syndrome (classic PSP)
  – Early onset postural instability and falls
  – Supranuclear vertical gaze palsy
  – Cognitive dysfunction
  – Much shorter disease duration
  – Younger age at death
Clinical variants (cont.)

• PSP-parkinsonism
  – Asymmetric onset of symptoms
  – Early bradykinesia
  – Tremor
  – Extra-axial dystonia
  – Moderate response to levodopa
Possible genetic basis

- Although PSP is usually sporadic, some studies have described a genetic cause

- H1 haplotype variant in the MAPT gene on chromosome 17 found in 95% of PSP patients (compared to 60% in general population)

- Other genes including MOPB, STX6, and EIF2AK3 also implicated in various studies
Hypothesis 1: Burst neurons in riMLF are responsible for slow saccades

Hypothesis 2: Omnipseuture neurons in RIP are responsible for slow saccades

Bhidayasiri R, et al.
Tauopathies

• Group of diseases defined by accumulation of tau
• Tau – microtubule binding protein that contributes to microtubule assembly and stabilization
• Different isoforms of tau exist - each referring to the number of copies of the part of the protein that binds it to the microtubules
• Significant overlap exists between phenotypes of various tauopathies
Histopathology

• PSP characterized by cerebral atrophy with pallor of substantia nigra and shrinkage of globus pallidus

• Neuronal loss and gliosis with abundant subcortical neurofibrillary tangles and neuropil threads

• Accumulation of insoluble hyperphosphorylated tau protein isoforms (increased four repeat tau)
http://www.highschoolbioethics.org/briefs/head-head-nfl-brain-injury
Pale locus cereleus

Pale substantia nigra

Medical knowledge

http://repository.countway.harvard.edu/xmlui/bitstream/handle/10473/4568/Progressive_Supranuclear_Palsy.pdf?sequence=2
http://repository.countway.harvard.edu/xmlui/bitstream/handle/10473/4568/Progressive_Supranuclear_Palsy.pdf?sequence=2
Penguin sign

Medical knowledge

Morning glory sign
Potential uses of MRI for diagnosis

• Oba, et al
  – Average midbrain area on mid-sagittal MRI significantly smaller with PSP than with PD, MSA, and normal controls (although some overlap with PSP and MSA)
  – Ratio of midbrain area to pons area significantly smaller in PSP than with PD, MSA, and normal controls

• Quattrone, et al
  – MR parkinsonism index = \([(P/M) \times (MCP/SCP)]\)
  – Value significantly larger with PSP (median 19.42) than in PD (9.40), MSA (6.53), and controls (9.21) with no overlap
Management

- No cure for PSP and current therapy usually ineffective
- Dopaminergic drugs can provide nominal or transient improvement
- Palliative therapy – PT, ST, walker, wheelchair, gastrostomy tube
- Ambien, botulinum toxin, AT
PSP vs Idiopathic Parkinson’s disease (PD)

• PSP may be indistinguishable from idiopathic PD in the early stages

• Reduced or attenuated response to dopaminergic medications

• Early postural instability and falls

• Tremors are rare with PSP

• Normal cardiac MIBG
Ocular motor apraxia

• Typically a congenital condition

• Acquired ocular motor apraxia much less commonly described in literature
  – Bilateral frontoparietal lobe lesions and infarcts
  – Cardiopulmonary surgery

• Loss of volitional saccades (especially horizontal) and smooth pursuit
Back to our patient

• Referred to Neurology for continued management and titration of dopaminergic medications

• MRI pending

• Ophthalmology planning on cataract surgery to help contrast sensitivity and reduce risk of falls
Take home points

• PSP is a rare neurodegenerative progressive disorder characterized by early postural instability and vertical gaze palsy

• Often misdiagnosed as PD – consider PSP in cases when ocular signs and early postural instability are prominent findings

• Diagnosis is made clinically although advances in MRI research may soon help in making an earlier diagnosis
Reflective practice

• This case allowed me the opportunity to see a classic presentation of the relatively rare entity, progressive supranuclear palsy. By taking care of this patient and educating myself about his disorder, I gained a deeper understanding of PSP and its closely related diseases. I believe our service did an outstanding job in accurately diagnosing the patient’s condition, educating him about the condition and our recommendations, and caring for him in a respectful and resourceful manner.
Core competencies

- **Patient care:** The case involved thorough patient care and attention to the patient's complaints. A sincere effort was made to urge patient to follow up with Neurology.

- **Medical knowledge:** This presentation allowed me to review the presentation, differential diagnosis, proper evaluation, and diagnostic criteria for PSP.

- **Practice based learning and improvement:** This presentation included a current literature search of developing and current diagnostic strategies for PSP.

- **Interpersonal and communication skills:** Every effort was made to communicate with the patient the importance of following up with Neurology.

- **Professionalism:** The patient was treated with respect at all times and was diagnosed in a timely manner.

- **Systems based practice:** Good communication between our service and Neurology ensured that the patient received proper management of his condition.
References


• Rucker J. Neural control and clinical disorders of supranuclear eye movements. ACNR. July 2012.
Thank you!

- Dr. Elmalem
- Dr. Calderon
- Patient and his wife