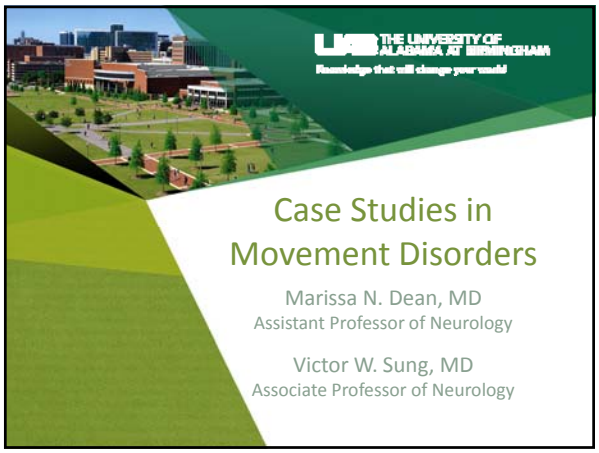

Case Studies in Movement Disorders

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Disclosures

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

Objectives

- Discuss phenomenology of movement disorders through case presentations.
- Provide a differential diagnosis for movement disorder cases.

Acknowledgments

- Patients and families for allowing the sharing of videos
- Juliana Coleman, MD for creating videos

Case 1: Wiggly toes

Case 1

- 53 yo RH woman with toe movements
- 3 years ago
  - Restlessness in bilateral feet
  - Began after starting trazodone
  - Involuntary movement of toes
  - Burning, tingling, and numbness in toes
- 2 years ago
  - Stopped trazodone – symptoms worsened
  - Worst at night, but also present during day
  - Can feel toes moving in shoes

Case 1 – additional history

- Meds tried
  - Ropinirole 0.5 mg BID -> minimal change in movements, no help with pain
- Medical history
  - Hypertension, hypothyroidism
- Family history
  - No known neurological disease or movement disorders.
- Social history
  - Smokes tobacco ½ ppd x 20 yrs

Case 1 - exam

- Reflexes
  - Grade 1 at knees, absent at ankles
- Sensation
  - Normal pinprick
  - Decreased vibration up to medial malleolus bilaterally
  - Decreased proprioception at toes bilaterally
- Muscle tone
  - Normal

Case 1 Video

Athetosis vs Pseudoathetosis

- Area of debate among MD specialists
- In theory, 'athetosis' is from BG lesions (almost solely associated with CP), and 'pseudoathetosis' is from proprioception loss
  - However, 'athetosis' in CP = 'chorea' and 'dystonia'
- Pseudoathetosis
  - Distal limbs
  - Writhing, slow, continuous involuntary movements
  - Patterned

Fahn et al, Principles and Practice of Movement Disorders, 2011; Abdo et al, *Nature Reviews* 2010

Work-up

- EMG/NCS BLE
  - BLE sensory polyneuropathy

Painful legs moving toes (PLMT)

- Uncommon disorder
  - Mainly described in case reports and case series
- Pain in one or more limbs
- Repetitive, non-rhythmic movement of toes
- Also,
  - Painful arms and moving fingers
  - Painful mouth and moving tongue - rare
  - Painless variants - rare

Hassan et al, *Neurology* 2012

PLMT

- Mean age at onset in 50s
- Mean age at presentation in 60s
- Possible women predominance
- Most commonly in legs
- Unilateral or bilateral
- Etiology
  - Mechanism unclear – most suspect some central involvement (central processing of peripheral nerve dysfunction)
  - Peripheral neuropathy, limb trauma, radiculopathy, cryptogenic

Hassan et al, *Neurology* 2012; Tocco et al, *MDCP* 2014

PLMT - treatment

- Pain is most bothersome symptom
- Difficult to treat – no evidence-based guidelines
- Poor response to medications
  - Gabapentin, pregabalin, clonazepam, dopamine agonists
- Botulinum toxin injections
- Spinal cord stimulator

Hassan et al, *Neurology* 2012; Tocco et al, *MDCP* 2014; Takahashi et al, *Pain* 2002

Case 1 - take home points

- Pseudoathetosis
  - Distal limbs
  - Writhing, slow, continuous involuntary movements
  - Patterned
- PLMT
  - Usually with peripheral etiology
  - Pain has poor response to treatments

Case 2:
Arm spasms

Case 2

- 62 yo RH woman
  - 7 years ago – tremor/spasm in left arm
  - Worsened over time
  - Now, can't type at work
  - Left hand found in weird positions
  - Symptoms worst in AM
  - Cannot tie shoes, play piano, button clothes
  - Stumbling more, left foot tends to drag/catch on objects

Case 2

- Speech
  - More stuttering, hesitations
- Memory
  - Worse with names, name recall
  - Leaves stove on and forgets – no longer using stove
  - Confusion in un-familiar environments, but quickly figures out where she is
  - Independent in basic ADLs

Case 2 – more history

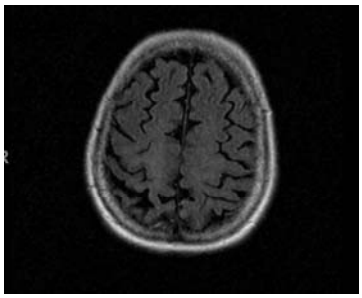
- Prior treatments
  - Valproic acid 1000 mg daily – no change
  - Cervical spine surgery for cervical stenosis – no change
  - PT – some improvement
- Medical history
  - C5-C6 spine surgery for cervical stenosis, asthma
- Family history
  - Dementia in maternal grandmother.

Case 2 - exam

- Muscle tone – normal
- Reflexes – normal
- Sensation – normal pinprick, vibration, proprioception
- Left arm extinction
- Agraphesthesia bilaterally

Case 2 Video

Case 2 – T2 FLAIR



Corticobasal syndrome (CBS)

- Neurodegenerative syndrome
- Atypical parkinsonian syndrome
- CBS – clinical syndrome with several etiologies (most commonly CBD)
- Corticobasal degeneration (CBD) – neuropathological disease
  - Cortical and striatal tau-positive lesions in glia and neurons

Dickson et al 2002; Armstrong et al, *Neurology* 2013

Probable CBS – diagnostic criteria

- Asymmetric (need 2):
  - Limb rigidity or akinesia
  - Limb dystonia
  - Limb myoclonus
- Need 2:
  - Orobuccal or limb apraxia
  - Cortical sensory deficit
  - Alien limb phenomenon

Armstrong et al, *Neurology* 2013

Probable CBD – diagnostic criteria

- Insidious onset with gradual progression
- Symptoms ≥ 1 yr
- Age ≥ 50 yo
- No family history of similar symptoms (2 or more)
- Probable CBS

- **Dementia frequently seen, but not included in diagnostic criteria.**

Armstrong et al, *Neurology* 2013

Imaging in CBS and CBD

- Asymmetric frontoparietal lobe atrophy
  - Premotor cortex
  - SMA (supplemental motor area)
  - Posterior superior frontal lobe

Boxer et al, *Arch Neurol* 2006

CBS/CBD - prognosis and treatment

- CBD – 6-8 years
- Mean age at onset – 64 yo
- No specific tx for CBS/CBD
  - Myoclonus – clonazepam, levetiracetam
  - Rigidity/akinesia/dystonia – levodopa, dopamine agonists, amantadine, baclofen, botulinum toxin
  - Memory – AchEI, memantine

Armstrong et al, *Neurology* 2013

Case 2 - take home points

- CBS
  - Atypical parkinsonism with more rapid progression
  - Prognosis 6-8 years
  - Asymmetric rigidity/akinesias, dystonia, and/or myoclonus + cortical sensory loss/alien limb

Case 3: Imbalance

Case 3

- 50 yo man – gait difficulty
  - 4 months ago – change in personality
    - Loud and talkative -> quiet in conversation
    - Lack of insight into this change
  - 3 months ago – balance problems began
    - Stumbling more
    - Double vision
    - Short term memory problems – forgetting prior events in the day (ex: brushing teeth)

Case 3

- 2 months ago – change in speech
  - Fragmented, only speaking in short phrases
  - Awkward while holding objects
  - Clumsy
  - Using cane for ambulation
- Within last month – mute and using a walker
  - Significant difficulty with all motor tasks
- Family reports fluctuating symptoms from day-to-day

Case 3 – more history

- Family history
  - Father died at 50 yo – alcohol abuse, liver cirrhosis, unable to walk prior to death
- Medical history
  - Appendectomy
- Meds – none
- Social history
  - High school graduate
  - Father abusive to mother, divorced, and left him when he was 6 yo
  - Used to drink ETOH heavily; none in >15 years

Case 3 - exam

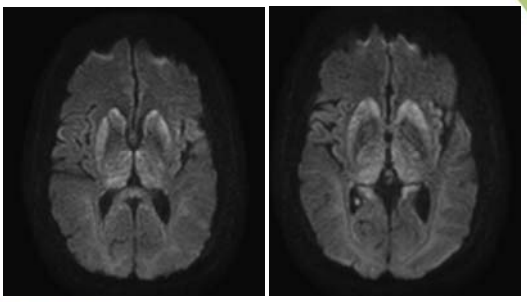
- Non-verbal
- Appears to follow some commands on the right, mostly consistent
- Muscle tone – severe rigidity in neck and extremities (R>L)

Case 3 - Video

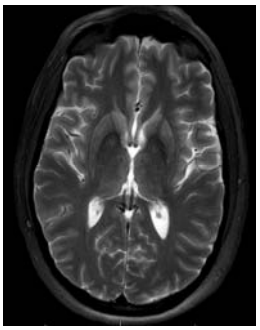
Case 3 – workup

- Labs
  - Thiamine – undetectable
- CSF
  - Glucose – 76 (116 serum)
  - Protein – 44
  - WBC – 1
  - RBC - 10
- EEG – mild slowing
- Imaging

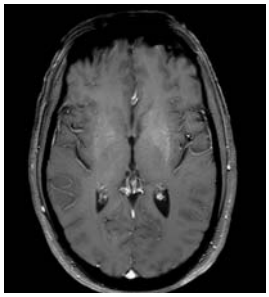
Case 3 - DWI

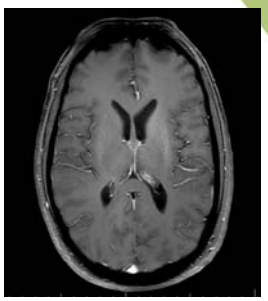


Case 3 – T2



Case 3 – T1 post-contrast





Case 3 – further workup

- Paraneoplastic/autoimmune encephalitis panel – negative
- CSF
  - Tau – positive
  - Protein 14-3-3 – positive
  - RT-QuIC – positive

Creutzfeldt-Jakob Disease (CJD)

- Neurodegenerative prion disease
- Rapidly progressive dementia with involuntary movements
- 70% die within one year
- Average age of onset in 60s

cdc.gov/prions/cjd

CJD subtypes

- Acquired, familial, or idiopathic
- Acquired (rare) – Kuru, bovine spongiform encephalopathy (variant CJD), iatrogenic CJD (corneal implants)
- Familial (10-15%)
- Idiopathic (85%) – AKA sporadic CJD

Fragoso et al 2017

Probable CJD – diagnostic criteria

- Rapidly progressive dementia + 2 (myoclonus, visual/cerebellar signs, pyramidal/extrapyramidal signs, or akinetic mutism)

  OR

  Neuropsychiatric disorder + RT-QuIC positive in CSF
- Need 1:
  - EEG – periodic sharp wave complexes
  - 14-3-3 positive in CSF (if disease <2 years)
  - DWI/FLAIR hyperintensity in caudate/putamen OR 2 cortical regions

cdc.gov/prions/cjd

Imaging in CJD

- Classic sCJD
  - MR – BG + cingulate/frontal/parietal lobes (cortical ribboning)
- Atypical sCJD (less frequent)
  - MR – BG + thalamus
- Familial CJD (PRNP gene mutations)
  - MR – similar to sCJD
- vCJD
  - MR – Pulvinar and hockey stick sign

Fragoso et al 2017

Our patient – probable CJD

- **Rapidly progressive dementia** + 2 (**myoclonus**, visual/cerebellar signs, pyramidal/extrapyramidal signs, or **akinetic mutism**)

  OR

  Neuropsychiatric disorder + RT-QuIC positive in CSF
- Need 1:
  - EEG – periodic sharp wave complexes
  - **14-3-3 positive in CSF (if disease <2 years)**
  - **DWI/FLAIR hyperintensity in caudate/putamen** OR 2 cortical regions

Our patient – imaging

- Classic sCJD
  - MR – BG + cingulate/frontal/parietal lobes (cortical ribboning)
- **Atypical sCJD (less frequent)**
  - **MR – BG + thalamus**
- **Familial CJD (PRNP gene mutations) – possible**
  - **MR – similar to sCJD**
- vCJD
  - MR – Pulvinar and hockey stick sign

Take home points

- CJD – rapidly progressive dementia within <12 mo
  - Sporadic CJD most common
    - 2 imaging patterns
    - CSF – RT-QuIC and 14-3-3
- Recognition of phenomenology can assist in diagnosis (akinetic mutism + myoclonus)

Case 4:
Left knee pain from fall

Case 4

- 56 yo RH woman with frequent falls
- 3 months ago – had fall and fell onto left knee
  - Went to ED for severe pain
  - SBP>180 and HgbA1c=12.6 (BG 321)
  - CT head done – interpreted as normal
  - Diagnosed with HTN and DMII
  - Discharged home

Case 4

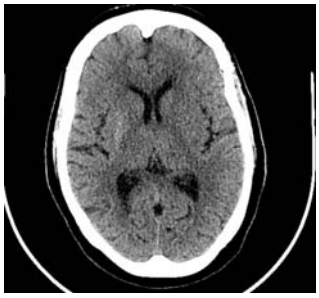
- 2.5 weeks later, presented to ED with involuntary movements x1 week
- Left leg and arm involuntary movements that began 2 days after a steroid injection into left knee
- Progressed in severity over past week
- Continuous movements – no alleviating factors

Case 4 – Video

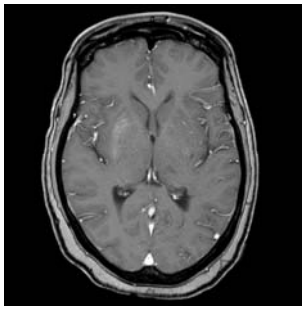
Chorea vs ballism

- Chorea – random, non-rhythmic, abrupt, rapid, un-sustained movements that flow from one body part to another
- Ballism – Chorea that affects a proximal joint (such as hip or shoulder) and produces large amplitude movements

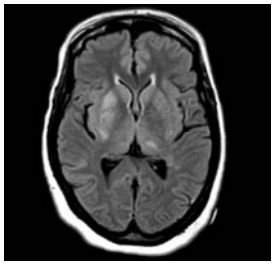
Case 4 – CTH first ED visit

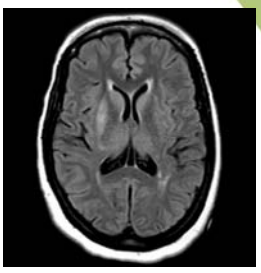


Case 4 – T1



Case 4 – T2 FLAIR





Case 4 – follow up

- Labs during admission
  - BG – 97
  - Heavy metal screen, autoimmune encephalopathy panel, UDS – negative
  - Vit b12, copper, ceruloplasmin – wnl
- Diagnosis?

Nonketotic hyperglycemia-induced hemichorea/hemiballism

- Seen in uncontrolled DM or as initial symptom of DM
- Slightly more common in women
- Mean age at onset 70 yo
- Age is greatest risk factor
- Average BG 300 at symptom onset
- Imaging – striatum hyperdense (CT) and hyperintense (MRI T1); T2 findings vary

Cosentino et al 2016

Nonketotic hyperglycemia-induced hemichorea/hemiballism

- Prognosis – usually good
- Most will have complete resolution of symptoms over time
- Treatments
  - dopamine antagonists (risperidone, olanzapine, haloperidol, etc.)
  - Clonazepam
  - Tetrabenazine, deutetrabenazine

Cosentino et al 2016

Take home points

- Hemichorea/hemiballism may be first presentation of DM
- Striatum – hyperdense on CT and hyperintense on MRI T1
- Movements usually improve with normalizing BG, but some may require treatment

Case 5a and 5b

- 2 videos of parkinsonism
  - Idiopathic PD
  - Functional parkinsonism (FMD)

Case 5a and 5b Videos

Functional parkinsonism

- Marked slowness with examined tasks, but normal casual tasks
- No cogwheel rigidity
- Pincer function preserved and lack of decrement
- 'huffing and puffing' sign
- Tremor – non-rhythmic, varying frequencies, same severity with action and at rest, entrainment, distractible

LaFaver and Espay, *Semin Neurol* 2017

Thank you!