Uncommon presentation of Common movement disorders

Case 1. A 63-year-old man with gait difficulty

Clinical Assistant Professor / Dallah Yoo, MD
Kyung Hee University Hospital, Seoul, Republic of Korea
• C.C. Progressive gait difficulty (O: 2YA, 61YO)
  • Cognitive impairment (O: 1YA, 62YO)
  • Recent frequent falling (63YO)

• Non-motor symptoms
  • Constipation/Hyposmia/RBD Sx. (+/+/-)
  • Depression (+)
Video (63YO)

- Explosive speech
- A fixed staring facial expression
- Vertical/Horizontal limitation of eye movement by verbal direction
- Up/Down gaze limitation by visual stimuli, which is overcome by VOR
- Bilateral bradykinesia, L>R
- Dysmetria on the left side
- Mild postural instability
- Unsteady gait with ataxia
1YA, 62YO

**18F-FP-CIT PET Brain MRI**

- Decreased DAT binding in the R>L putamen
- Mild atrophy in the midbrain and cerebellum

**Brain MRI**
• Cognitive screening evaluation (present, 63YO)

• K-MMSE (22/30 points)
  • orientation to time (3/5 points)
  • orientation to place (4/5 points)
  • three word registration (3/3 points)
  • attention and calculation (3/5 points)
  • three word recall (1/3 points)
  • language (7/8 points)
  • visual construction (pentagon copying, 1/1 point)
Clinical Diagnosis

Probable PSP-RS

- Age at onset: 61
- Progressive gait difficulty
- Early falls
- Supranuclear gaze palsy (SNGP)

TABLE 2. Core clinical features

<table>
<thead>
<tr>
<th>Levels of Certainty</th>
<th>Ocular Motor Dysfunction</th>
<th>Postural Instability</th>
<th>Akinesia</th>
<th>Cognitive Dysfunction</th>
</tr>
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<tbody>
<tr>
<td>Level 1</td>
<td>01: Vertical supranuclear gaze palsy</td>
<td>P1: Repeated unprovoked falls within 3 years</td>
<td>A1: Progressive gait freezing within 3 years</td>
<td>C1: Speech/language disorder, i.e., nonfluent/agrammatic variant of primary progressive aphasia or progressive apraxia of speech</td>
</tr>
<tr>
<td>Level 2</td>
<td>02: Slow velocity of vertical saccades</td>
<td>P2: Tendency to fall on the pull-test within 3 years</td>
<td>A2: Parkinsonism, akinetic-rigid, predominantly axial, and levodopa resistant</td>
<td>C2: Frontal cognitive/behavioral presentation</td>
</tr>
<tr>
<td>Level 3</td>
<td>03: Frequent macro square wave jerks or “eyelid opening apraxia”</td>
<td>P3: More than two steps backward on the pull-test within 3 years</td>
<td>A3: Parkinsonism, with tremor and/or asymmetric and/or levodopa responsive</td>
<td>C3: Corticobasal syndrome</td>
</tr>
</tbody>
</table>
• The 2017 MDS-PSP clinical diagnostic criteria do NOT provide PSP-C.
  • Very Rare phenotype
  • No specific features to allow antemortem diagnosis
  • Risk including patients with MSA-C or adult-onset cerebellar ataxias

• Proposed diagnostic criteria for **PSP-C**

  (A) slowly progressive course,
  (B) onset>40 years,
  (C) supranuclear gaze palsy,
  (D) truncal and limb ataxia **within 2 years after symptom onset**, and
  (E) postural instability with falls within 2 years after symptom onset

  • Probable PSP-C requires A+B+C+D+E
  • Possible PSP-C requires A+B+D+E

*Exclusion criteria*: marked dysautonomia and “hot cross bun” sign on a brain MRI

Shimohata, 2015
An Autopsy Study of PSP-C

**Frequency in pathologically proven PSP-C**

- 3 of 22 (14%, Japan)
- 0 of 30 (0%, Austria); 2 of 30 (6.7%) developed cerebellar signs in late stages
- 0 of 100 (0%, Europe and Canada)
- 5 of 1085 (0.5%, USA)

**Pathologic features of PSP-C**

- Distinctive Purkinje cell loss
- Greater frequent of tau(+) inclusions in Purkinje cell
- More severe tau pathology in the cerebellar dentate nu.

---

**Purkinje cells**

**Dentate Nu.**

Jellinger, 2010

Koga, 2015
Clinical features

- **PSP-C**
  - Gait disturbances a/w truncal ataxia
  - Men>Women
  - Falls ± SNGP
  - Very rarely RBD or OH

- **PSP-C compared with MSA-C**
  - Higher age at onset
  - Early falling
  - Common SNGP
  - No remarkable atrophy of cerebellum in early stage

Ando, 2019
Uncommon presentation of common movement disorders

Case 2. 57-year-old man with asymmetric ataxia

Clinical Assistant Professor / Jong Hyeon Ahn, MD
Samsung Medical Center, Seoul, Republic of Korea
Case 2.

- M/57
- Chief complaint: Progressive gait disturbance, right hand clumsiness
- Onset: 6 months ago

- RBD +, Hyposmia -
- Constipation -
- Urinary Sx -
- Orthostatic dizziness -
- Erectile dysfunction -

- Family history: none
- Past medical history: Hypertension on medication
Case 2.
Case 2.
Case 2.

- Problem list
  - Slowly progressive right-sided dominant ataxia
  - With the unilateral MCP sign
  - With asymmetric cerebellar atrophy on the Brain MRI
  - RBD +, but no dysautonomia
Differential diagnosis of the MCP sign

• The MCP sign in degenerative cerebellar ataxia: bilateral and symmetric
Asymmetric / Unilateral MCP sign

• Suggesting other etiology than degenerative cerebellar ataxia

Multiple sclerosis  Progressive multifocal leukoencephalopathy  Low grade astrocytoma  Cavernoma
Asymmetric / Unilateral MCP sign

• Suggesting other etiology than degenerative cerebellar ataxia

Anterior inferior cerebellar artery (AICA) infarct

Wallerian degeneration after left pontine infarct
Case 2. Investigations

- Investigations
  - Spinal tapping: no evidence for demyelinating disease or infection
  - CSF cytology: negative
  - Paraneoplastic / Antineuronal Abs: negative

- Genetic testing
  - FMR1: negative
  - SCAs 1, 2, 3, 6, 7, 8, 17: negative
  - DRPLA: negative

- Head-up tilt test: Normal, (Orthostatic hypotension, OH; -)
Case 2. Investigations

- FP-CIT-PET

No reduction of FP-CIT binding in bilateral striatum
Case 2. Investigations

• Ataxia was progressed, but still asymmetric

• He developed a following dysautonomic symptoms 1.5 years after the first brain MRI
  • OH + with orthostatic dizziness
  • Urinary frequency and urgency +
  • Constipation +
  • Erectile dysfunction +
Case 2. Investigations

• Follow-up brain MRI (1.5 years after first brain MRI)
Case 2.

• Late onset, progressive cerebellar ataxia and dysautonomia
• MRI findings suggest MSA-C

• Final diagnosis
  • Multiple system atrophy - cerebellar type
    presenting with marked asymmetry and unilateral MCP sign
Multiple system atrophy

• MSA has relatively **symmetric symptoms** compared to Parkinson’s disease
• But the **parkinsonism** of MSA **can be asymmetric**

Second consensus statement on the diagnosis of multiple system atrophy

**Parkinsonism.** Most MSA patients develop parkinsonism (bradykinesia with rigidity, tremor, or postural instability) at some stage. The tremor is usually irregular and postural/action, often incorporating myoclonus, but a classic pill-rolling rest tremor is uncommon. **The parkinsonism can be asymmetric.** Postural instability, as
Asymmetric parkinsonism in MSA

• 5 cases of MSA-P with marked asymmetry
  • Marked asymmetry in atypical parkinsonism suggests alternative diagnosis like CBS.
  • Autonomic features, preserved cognition and respiratory difficulties
    -> Suggest MSA than CBS

Batla et al. Parkinsonism Relat Disord. 2013
Asymmetric parkinsonism in MSA

- MSA-P with marked asymmetry
  - 50/M, 2 years history of the left-hand clumsiness
  - RBD +
  - Orthostatic Hypotension +
  - Urinary frequency +, incontinence +, Impotence +
Asymmetric “Ataxia” in MSA

• To the best of our knowledge, MSA-C with marked asymmetric ataxia or unilateral MCP sign has yet not been reported.

• Careful history taking, neurologic examination, and follow-up of the patient are required to determine signs and symptoms suggestive of MSA, such as RBD, autonomic dysfunction.
Uncommon presentation of Common movement disorders

Case 3. A 63-year-old man with eye opening difficulty

Clinical Assistant Professor / Dallah Yoo, MD
Kyung Hee University Hospital, Seoul, Republic of Korea
• C.C. eye opening difficulty (O: 1YA, 62YO)
  • Rt. hand clumsiness (O: 6MA, 63YO)
  • Recent gait difficulty (63YO)

• Non-motor symptoms
  • Olfactory dysfunction/Constipation/RBD Sx. (+/-/-)
  • Urinary frequency/Nocturia/RU sense (+/+/+)
  • Orthostatic dizziness (-)
  • Subjective cognitive decline(-)
Video (63YO)

- Inability to voluntary eyelid opening after lid closure
- Involuntary forced eyelid closure (-)
- No definite Up/Down gaze limitation
- Hypokinetic speech
- Hypomimia with his mouth open
- Bilateral bradykinesia
- Reduced arm swings, L>R
- Slight circumduction of the left leg
- Normal postural reflex
Severely decreased DAT binding in the caudate and putamen

No prominent midbrain atrophy

Diffuse cerebral cortical atrophy, especially in F-T lobes

Present, 63YO
• **Repetitive nerve stimulation test**
  • No abnormal incremental/decremental responses

• **Video oculography**
  • Suspicious upward saccadic slowing
• Cognitive screening evaluation

• K-MMSE (23/30 points)
  • orientation to time (4/5 points)
  • orientation to place (5/5 points)
  • three word registration (3/3 points)
  • attention and calculation (1/5 points)
  • three word recall (2/3 points)
  • language (7/8 points)
  • visual construction (pentagon copying, 1/1 point)
Clinical Diagnosis

Suggestive of PSP-OM or PSP-P

- Age at onset: 62
- ALO
- Parkinsonism, akinetic-rigid>tremor

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Video

Improved ALO after Clonazepam 0.75mg a day
No response to Levodopa 150mg, Baclofen 30mg, or Nortriptyline 30mg a day
Apraxia of lid opening in Parkinsonism

**ALO**, “a non-paralytic motor abnormality characterized by the patient’s difficulty in initiating the act of lid elevation.”

by Goldstein and Cogan in 1965

The frequency of ALO

- Prevalence: 59/1000,000 in general population
- 2.1% of patients with parkinsonism (PSP, 33.3%; PD, 0.7%)

**ALO as initial presentation in PSP**

- Rare
- Middle to late stage (>4Y of disease duration)

Hamedani, 2017
Phokaewvarangkul and Bhidayasiri, 2019
• Pathophysiology of ALO

• Excess supranuclear levator palpebrae inhibition, 
• Pretarsal motor persistence, or both

• Hypometabolism of the cingulate and SMA

Chung, 1996
Suzuki, 2003
Hamedani, 2017
- **Etiology**
  - Idiopathic focal dystonia
  - Iatrogenic; drug-induced (antidepressant, antipsychotics, levodopa, DBS)
  - Genetic; DYT1
  - Structural; traumatic brain injury of the midbrain, BG, thalamus, cerebellum
  - **Neurodegenerative**: PSP>MSA>PD, CBS, ALS, FTD, HD, SCA2/3, WD

- **Treatment**
  - Botulinum toxin injections (pretarsal ocularis oculi muscle)
  - Eyelid crutches or goggles
  - Trial of levodopa or other medications
    - Anticholinergics
    - Aripiprazole
    - methylphenidate

Smith, 1994
Suzuki, 2003
Hamedani, 2017
Uncommon presentation of common movement disorders

Case 4. 60-year-old man with involuntary jaw opening

Clinical Assistant Professor / Jong Hyeon Ahn, MD
Samsung Medical Center, Seoul, Republic of Korea
Case 4.

- 60/M
- Chief complaint: Involuntary jaw opening, recurrent tongue biting
- Onset: 12 months ago

- Slowly progressive
- He had difficulty eating and speaking

- Past medical history: None
- Medication/Toxin exposure: None
- Family history of gait disturbance
Case 4.
Case 4.
Case 4.

• Problem List
  • Late onset, slowly progressive jaw opening and lingual dystonia
  • Hypermetric saccade
  • Autosomal dominant family history of gait disturbance
Case 4.

Differential diagnosis of oromandibular dystonia/dyskinesia

- Drug induced / Toxic
- Neurodegenerative disease
  - Huntington's disease
  - Chorea-acanthocytosis
  - PKAN
  - Neuroferritinopathy
  - Kufor Rakeb disease
  - Wilson disease
  - Ataxia-telangiectasia
  - Lesch-Nyhan syndrome
  - Gaucher disease
  - Cerebrotendinous xanthomatosis
- Paraneoplastic / Autoimmune
  - Anti-Ma2, NMDA, CRMP5...
- DYTs
  - TOR1A, TAF1, GCH1, THAP1, PRKRA, ANO3, GNAL..
- SCAs
  - SCA1, 2, 3, 8, 36...
Case 4.

- Genetic testing revealed an increased trinucleotide repeats in \textit{ATXN-2} gene (22/40)

- Final diagnosis
  - \textit{Spinocerebellar Ataxia Type 2}
    - presenting with jaw opening and lingual dystonia
Spinocerebellar ataxia 2

• 2nd most common subtype of SCA worldwide
• Age of onset: second – third decade

• Common phenotype
  • Gait disturbance is most common presenting symptom (97%)
  • Ataxia, early saccade slowing, tremor

• Various phenotypes
  • Peripheral neuropathy, parkinsonism, cognitive decline
  • Resting tremor (14.2%), Dystonia (14.2%), Myoclonus (13.7%), rigidity (7.4%), chorea (6.8%)
Dystonia in SCAs

- During overall disease course: **19%**
- Dystonia as a presenting symptom: < **5%**

<table>
<thead>
<tr>
<th>Total No. of Patients</th>
<th>140 (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper-limb dystonia</td>
<td>66/140 (47%)</td>
</tr>
<tr>
<td>Writer’s cramp</td>
<td>8/66 (12%)</td>
</tr>
<tr>
<td>Lower-limb dystonia</td>
<td>31/140 (22%)</td>
</tr>
<tr>
<td>Cervical dystonia</td>
<td>42/140 (30%)</td>
</tr>
<tr>
<td>Blepharospasm</td>
<td>10/140 (7%)</td>
</tr>
<tr>
<td>Craniofacial dystonia</td>
<td>5/140 (4%)</td>
</tr>
<tr>
<td>Lingual dystonia</td>
<td>3/140 (2%)</td>
</tr>
<tr>
<td>Dystonia NOS</td>
<td>116</td>
</tr>
</tbody>
</table>


35/M, genetically confirmed SCA3
Dystonia in SCA2

- About **14%** of SCA2 patients have dystonia (Rossi, 2014)

- Types of dystonia in SCA2
  - **Cervical dystonia** (Boesch, 2007) and **craniofacial dystonia** (Markovic, 2015) were the most common types of dystonia in SCA2
  - Generalized, cervical, craniofacial, lingual, writer’s cramp, and foot

- Jaw-opening and lingual dystonia
  - Several cases have been reported in SCA2 (Markovic 2015, Antenora 2014)
  - But also reported in SCA 1, 8 and 36
Conclusion

• In SCAs, dystonia can be seen as a presenting symptom.

• Careful examination, including that of eye movements, is important for patients with dystonia.

• In patients with ataxia and dystonia, SCAs should be considered.
Uncommon presentation of common movement disorders

Case 5. 63 year-old man with neck tremor

Assistant Professor / Ji Young Yun
Ewha Womans University, Seoul, Republic of Korea
Chief complaint

• Neck tremor
  • Onset: 1 month ago
  • Distribution: Anterior and lower neck
  • No interference with his ability to speak, chew or swallow

• Referred from otolaryngologist
Past history

• DM/HTN/Tbc/Hepatitis (-/-/-/-)

• Dyspepsia
  • Taking medication for 3 months
• Anterior-lower neck tremor at rest
  • Rhythmic up-and-down oscillating movement of the anterior-lower neck at rest
  • Frequency: Approximately 4~5 Hz
  • Appeared when he closed his jaw
  • Disappeared when he began to speak or protrude his tongue
  • No chin tremor or palatal tremor

• No bradykinesia, no rigidity
• Other neurological findings were unremarkable
Laboratory findings

- T3: 81.1
- T4: 8.8
- TSH: 1.14
- Blood urine nitrogen: 12
- Creatinine: 0.64
Differential diagnosis

- R/O Atypical cervical tremor
- R/O Parkinsonian tremor
- R/O Drug-induced tremor
• Medication for dyspepsia from other clinic
  • Rabeprazole 20mg/day
  • **Levosulpiride 75mg/day**
  • Tiropramide 0.3g/day
  • Rebamipide 300mg/day

• Levosulpiride was discontinued.
After the cessation of levosulpiride, the tremor had disappeared in two days.
Levosulpiride related movement disorders

- Clinical features
  - Parkinsonism (93.4%)
  - Tardive dyskinesia (9.9%)
  - Isolated tremor (3.3%)
    - Resting tremor on tongue, jaw and both feet
    - Postural tremor on both arms

- Persisted after withdrawal of levosulpiride
  - Parkinsonism in 48.1%
  - Dyskinesia in 66.7%
  - Isolated tremor in 0%

Levosulpiride-induced resting neck or orolingual tremor

Drug-Induced and Psychogenic Resting Suprahyoid Neck and Tongue Tremors

Jong Sam Baik, MD, PhD,1 Chul H. Lyoo, MD, PhD,2 Jae H. Lee, MD,2 and Myung Sik Lee, MD, PhD2*

1Department of Neurology, Sanggye P产学研 Hospital, Inje University College of Medicine, Seoul, Korea; 2Department of Neurology, Youngdong Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Video

Levosulpiride-Induced Resting Orolingual Tremor

Levosulpiride is a benzamide derivative used in the treatment of dyspepsia.1 Because it exerts its pharmacologic activity mainly by blocking dopaminergic D2 receptor activity, levosulpiride can cause extrapyramidal symptoms (EPS), most of which are generalized parkinsonism.2,3 We report a

mix, and benign prostate hypertrophy. During the most recent 2-month period, he took levosulpiride for gastroesophageal reflux. He had no history of trauma, cerebrovascular disease, or exposure to neuroleptics. Family history was not remarkable. On neurological examinations, his speech and cranial nerve function tests were normal. Motor and sensory function tests were normal. The deep tendon reflexes were hyporeactive, but symmetric bilaterally. The plantar responses were flexor bilaterally. His gait and postural reflexes were normal. There was minimal bradykinesia and rigidity, but no kinetic or resting tremor in his arms. There was a 4 to 5 Hz rapid rhythmic movement of the anterior upper neck at rest. There was no audible ear click. When he opened his mouth, no tremor of the tongue or palate was noted.


Conclusion

• Diagnosis: Levosulpiride-induced neck tremor

  • Levosulpiride can induce isolated neck tremor at rest without other parkinsonian features.

  • This isolated neck tremor can be reversible after the withdrawal of levosulpiride.
Uncommon presentation of common movement disorders

Case 6. 16 year-old girl with gait problem

Assistant Professor / Woong-Woo Lee (Woody)
Nowon Eulji Medical Center, Seoul, Republic of Korea
Case (F/16)

- F/16 with gait disturbance
- abnormal posturing since early childhood
- started in the lower limbs and spread upwards with age
- better in the morning and worsened over time
- psychomotor delay (+)
- development delay (+)
- depression with antidepressant

- Family history
  - no relevant history for neurodevelopmental disorders

- Family history
Mental: alert, oriented

CNE:
- EOM: full w/o nystagmus
- otherwise, no remarkable findings

Motor: all Gr V

Sensory: symmetric, intact

DTR:
(In the lower limbs)
- ankle clonus
- brisk tendon reflexes

Cerebellar function test: intact

Gait: video clip
Workup
- Sustained muscle contractions causing twisting, abnormal posturing, patterned movement ➔ **Dystonia**

- Distribution and temporal pattern
  : from lower extremities to trunk and upper extremities
  ➔ **Progressive, Generalized dystonia**
  : better in the morning and worsened over time
  ➔ **Diurnal fluctuation**

- Age at onset: **early childhood**

- Other signs
  - other movement disorders
    : parkinsonism (-), ataxia (-), tremor (-), chorea(-), myoclonus(-)
  - other neurological and systemic manifestations
    : psychomotor delay and developmental delay
    : depression with antidepressant
    : ankle clonus and brisk DTR
Dramatic response to L-dopa!
(4 mg/kg/day)
Targeted gene panel sequencing

- heterozygous missense variant of GCH1 (c.539A>C, p.Gln180Pro)

- No pathological mutations in the genes known to be associated with DRD, including the TH and SPR genes.

- No other variants suggest compound heterozygosity of GCH1.
DRD and BH4

TH deficiency
- Dopamine/NE deficiency:
  - L-dopa responsive
  - 'No' serotonin deficiency

BH4 deficiency
- Dopamine/NE deficiency:
  - L-dopa responsive
  - Serotonin deficiency

L-dopa

TH

AAPC

Dopamine

Serotonin

AADC deficiency
- Dopamine/NE deficiency:
  - mostly L-dopa non-responsive
  - Serotonin deficiency
**Dystonia**

<table>
<thead>
<tr>
<th>Age at onset</th>
<th>early childhood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body distribution</td>
<td>generalized dystonia (trunk + 4 extremities)</td>
</tr>
<tr>
<td>Temporal pattern</td>
<td>progressive and diurnal fluctuating pattern</td>
</tr>
<tr>
<td>Associated features</td>
<td>psychomotor delay and developmental delay depression with antidepressant ankle clonus and brisk DTR</td>
</tr>
</tbody>
</table>

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**Typical DRD**

- **Symptoms**
  - Dystonia
  - Diurnal fluctuation

- **Response to therapy**
  - Dramatic L-dopa response

- **Complication or additional neurological deficits**
  - Motor complications
    - Some dyskinesias
  - Parkinsonism
  - Others

**Atypical features**

- Earlier onset than DRD
  - Such as neonatal onset

- More severe motor phenotypes
  - Such as poor sucking, swallowing difficulties, severe hypotonia

- Not dramatic response to L-dopa

- **Non-motor features**
  - Convulsions (grand mal or myoclonic attacks), psychomotor retardation, mental retardation, depression, drowsiness, irritability, recurrent hyperthermia without infections, ptosis (a sign of catecholamine deficiency)
### Table: DRD, DRD-plus, DRD look-alike

<table>
<thead>
<tr>
<th>Previous name</th>
<th>Previous definition</th>
<th>New definition</th>
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<tr>
<td>DRD</td>
<td>A syndrome of selective nigrostriatal dopamine deficiency caused by genetic defects in the dopamine synthetic pathway without nigral cell loss</td>
<td>A group of non-neurodegenerative disorders by genetic defects involving nigrostriatal dopaminergic system with cardinal manifestations (namely, DRD phenotype)</td>
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<tr>
<td>DRD-plus</td>
<td>A group of disorders caused by genetic defects in the dopamine synthetic pathway without nigral cell loss that have features of DRD ‘plus’ those features that are not seen in DRD</td>
<td>A group of non-neurodegenerative disorders by genetic defects involving nigrostriatal dopaminergic system with dopa-responsiveness plus additional features (namely, DRD-plus phenotype) that are not seen in DRD</td>
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**DRD look-alike**

- Oculogyric crisis, Mental retardation

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*‘PLUS symptoms’ in DRD-plus*

- Infantile onset, developmental delay, psychomotor retardation, seizure, hypotonia, drowsiness, recurrent hyperthermia, ptosis, cerebellar dysfunction, poor responsiveness to levodopa or other dopaminergic drugs.

(Lee, Jeon, and Kim, JKMS, 2018)
(Hoffmann et al., Ann neurol 2003)
• Motor outcomes according to the enzyme defect

Genotype-Phenotype correlation

(Kim, Jeon, and Lee, MDCP, 2016)
Depending on severity of enzymatic defect

(Furukawa et al., *Ann Neurol* 1998)
• L-dopa should be tried on dystonic patients with diurnal fluctuation.

• GCH1 mutation is the most common genetic cause resulting in DRD phenotype.

• If a patient with L-dopa responsive dystonia has additional features which is not common in classic DRD, DRD-plus should be considered.

• Uncommon points in this case
  • Clinically, this case refers to DRD-plus phenotype. (DRD + additional presentations*)
  • However, genetically, the final diagnosis was made as AD GCH1 mutation, which seldom shows DRD-plus phenotype.

*psychomotor/developmental delay, depression, and increased DTR
Uncommon presentation of Common movement disorders

Case 7. A 79-year-old woman with hemichorea

Clinical Assistant Professor / Dallah Yoo, MD
Kyung Hee University Hospital, Seoul, Republic of Korea
• C.C. R hemichorea (O: 2016.12.)
  • Lt. STN-Thalamus, hypertensive intracerebral hemorrhage (2016.11.24.)
  • After one month from ICH
Symptomatic pharmacological management

- **2017.02.-09.**
  - Risperidone 4mg bid
  - Haloperidol 6mg tid
  - Aripiprazole 5mg tid
  - Valproic acid 600mg tid
  - Topiramate 25mg tid
  - Levetiracetam 250mg bid
  - IV Amantadine for 2 weeks

- **2017.10.**
  - Nortriptyline 10mg bid
  - Bromocriptine 1.25mg bid
  - Levetiracetam 250mg bid
  - Methylphenidate 10mg bid

- **2018.11.**
  - Quetiapine 25 tid add-on

- **2018.12.**
  - Levodopa 75 tid (mild parkinsonism)

- **2021.3.**
  - Levodopa 100 tid
  - Methylphenidate 20 bid
  - Levetiracetam 500 bid
  - Quetiapine 37.5tid
• Medication-refractory post-stroke hemichorea

• Decision to Lt. **GPi deep brain stimulation (DBS)**
  - Old age (79 years old)
  - Patient willingness to undergo surgical treatment
  - Caregiver’s support
  - Preserved cognitive function; K-MMSE 25/30 (<6 years of education)
  - Overall good functional status
  - No other comorbidities
Video
GPi-DBS in hemichorea/ballism (HCB)

- HCB, a disorder primarily of the subthalamic nucleus (STN)
  - Thalamic disinhibition via decreased GPi firing

![Diagram of neural pathways involving cerebral cortex, supplementary motor area, premotor area, primary motor area, striatum, ventral anterior/ventral lateral (VA/VL) thalamus, substantia nigra pars compacta (SNpc), globus pallidus externus (GPe), subthalamic nucleus (STN), and substantia nigra pars reticulata (SNr).]

**Table 1.** Review of pallidal neurophysiology.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
<th>Number of units</th>
<th>Firing rate mean ± SE (Hz)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PD</td>
<td>10</td>
<td>101</td>
<td>95.2 ± 2.3</td>
<td>Starr et al.(^{15})</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>14</td>
<td>46.1 ± 7.8</td>
<td>Oyama et al.(^{6})</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>188</td>
<td>89.9 ± 3.0</td>
<td>Tang et al.(^{14})</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>200</td>
<td>74 ± 1.2</td>
<td>Hutchison et al.(^{14})</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>13</td>
<td>96 ± 8</td>
<td>Suarez et al.(^{12})</td>
</tr>
<tr>
<td>Dys</td>
<td>22</td>
<td>302</td>
<td>55.3 ± 1.3</td>
<td>Starr et al.(^{15})</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>26</td>
<td>50 ± 4.0</td>
<td>Vitek et al.(^{13})</td>
</tr>
<tr>
<td>HD</td>
<td>2</td>
<td>39</td>
<td>81.8 ± 4.3</td>
<td>Tang et al.(^{14})</td>
</tr>
<tr>
<td>HB</td>
<td>1</td>
<td>17</td>
<td>33.7 ± 5.1</td>
<td>Vitek et al.(^{13})</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>13</td>
<td>30 ± 5</td>
<td>Suarez et al.(^{12})</td>
</tr>
<tr>
<td>HC-HB</td>
<td>1</td>
<td>12</td>
<td>53 ± N/A</td>
<td>Capelle et al.(^{7})</td>
</tr>
</tbody>
</table>

Postuma, 2003
Ramirez-Zamora, 2018
• Cases of GPi-DBS in Medication-refractory HCB

<table>
<thead>
<tr>
<th>Author</th>
<th>Hasegawa</th>
<th>Capelle</th>
<th>Genko Oyama</th>
<th>Xie</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>2009</td>
<td>2011</td>
<td>2014</td>
<td>2014</td>
</tr>
<tr>
<td>Age at op.</td>
<td>56</td>
<td>53</td>
<td>44</td>
<td>22</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>From Sx. to Op.</td>
<td>3 years</td>
<td>1 year</td>
<td>1 month</td>
<td>4 years</td>
</tr>
</tbody>
</table>

• Age: 22-56
• Major causes: stroke
• Duration between symptom to operation
  • 2 weeks-20 years
• Follow-up period after Op.: ~28 months
• Heterogenous outcomes
  • Purposeful usage to completely eliminated
• Incidence of refractory post-stroke HCB
  • 0.04% in a large series

<table>
<thead>
<tr>
<th>Author</th>
<th>The case</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>2021</td>
</tr>
<tr>
<td>Age at op.</td>
<td>79</td>
</tr>
<tr>
<td>Sex</td>
<td>F</td>
</tr>
<tr>
<td>From Sx. to Op.</td>
<td>4 years</td>
</tr>
<tr>
<td>Location of lesions</td>
<td>R STN, VL, SN</td>
</tr>
<tr>
<td>Cause</td>
<td>stroke (hemorrhage)</td>
</tr>
<tr>
<td>Op.</td>
<td>R GPI-DBS</td>
</tr>
<tr>
<td>F/U after op.</td>
<td>~ 2 weeks</td>
</tr>
</tbody>
</table>

Ghika-Schmid, 1997