

# 30 yo Japanese man with difficulty writing

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- 7 yo: Difficulty writing with his R hand.
  - Muscles felt tight. Held arm out with wrist extended.
  - Had occasional tremors that he could suppress
  - Able to hold chopsticks without problems.
- 12 yo: Gave up piano.
- 17 yo: Noted similar problem writing with the L hand.
  - Had neurosurgery in Japan with resolution of tremors and dystonia.
- 22 yo:
  - Dystonia gradually worse in the LUE and RUE dystonia returned.
- 28 yo:
  - Saw neurologist at UCSF. Started Sinemet.
  - Quit after 1.5 m due to fatigue and lack of effect.
  - Tried muscle relaxant and chiropractor with improved range of motion and decreased dystonia.
- 30 yo:
  - When excited, starts to stutter
  - Sense of restlessness

## Past Medical History

Tension headache

## Medications

Tylenol prn

## Social History

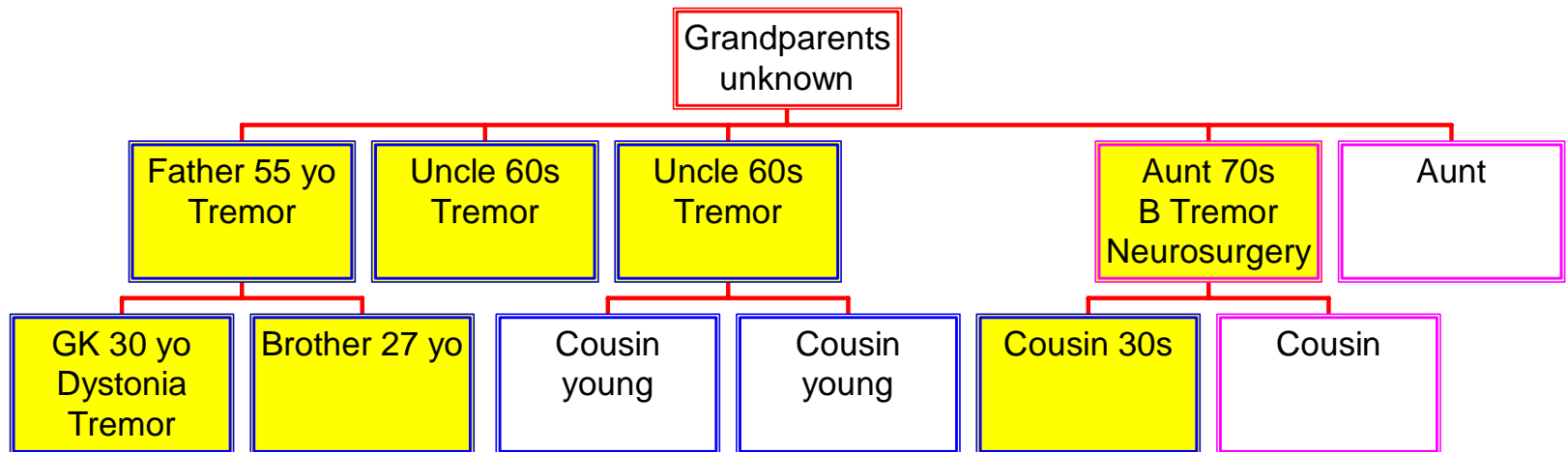
No tobacco, occasional EtOH, no recreational drugs.

Computer programmer for Adobe Systems for 3 yrs.

Business BS from SF State.

Came to US when 19 yo.

# Family History



# Physical Exam

- MS: MMSE 30/30
- CN: Normal and without dystonia
- M:
  - Normal tone, bulk, strength, reflexes, flexor plantar responses
  - Moderate amount of limb dystonia LUE>RUE
  - No truncal dystonia. No tremor or choreoathetosis
- S,CB,Gait,Romberg normal

Brief Cranial Nerve Exam

Upper Extremity Dystonia

February 20, 2000



# Rapid Alternating Hand Movements



Handwriting

February 20, 2000



Gait and Posture

February 20, 2000



# Rapid Alternating Hand Movements

June 5, 2000



# Gait and Posture

June 5, 2000



## MRI of the Brain

- Small left basal ganglia T2 hyperintense lesion
- No cerebral or basal ganglia atrophy

## Summary

- Onset during first decade of life
- Dystonia and tremor in RUE first
- Spread to LUE as well as trunk, ?bulbar
- Normal neurologic exam other than dystonia
- MRI of the brain normal except for L thalamotomy
- Affected family members, autosomal dominant
- Sinemet and EtOH did not help.

# DDx

- “Idiopathic” torsion dystonia
  - DYT1 early onset, limb onset (Torsin A)
  - DYT2 autosomal recessive dystonia in Gypsies
  - DYT3 X-linked dystonia/parkinsonism
  - DYT4 whispering dysphonia w Wilson ds in Australia
  - DYT5 dopa-responsive dystonia (GTP cyclohydrolase I)
  - DYT6 craniocervical dystonia
  - DYT7 torticollis
  - Others
- Hereditary autosomal dominant myoclonus dystonia (D2R/chromosome 11, chromosome 7)
- Rapid-onset dystonia parkinsonism (chromosome 19)

## DDx (Less Likely)

- Heredodegenerative diseases (Huntington, Wilson, Parkinson, Hallervorden-Spatz, striatopallidodentatal calcification, others)
- Dystonia musculorum deformans
- Metabolic disorders (kernicterus, hepatocerebral degeneration, lysosomal storage ds, etc.)
- Medications (phenothiazine, haloperidol, others)
- Poisoning (manganese)
- Hypoxia, stroke
- Head trauma

### Idiopathic Torsion Dystonia DYT1

1. Early onset (<28 yo)
2. Limb
3. Spread to other limb and trunk
4. Normal exam except for dystonia
5. Normal MRI of the brain

### Autosom Dom Myoclonus Dystonia

1. Onset first or second decade
2. Neck, arm > face, trunk > LE
3. Non-progressive
4. Symptoms relieved by alcohol
5. Possible association with alcoholism and psych ds

### Dopa-Responsive Dystonia

1. Onset 4-8 yo, F>M
2. Legs affected first
3. Spread to arm, trunk, bulbar within 5 yrs
4. Parkinsonian feature early
5. Diurnal variation
6. Dramatic response to Sinemet

### Rapid-Onset Dystonia-Parkinsonism

1. Limb dystonia first
2. Acute onset of dysarthria, dysphagia, dystonic spasms, bradykinesia, postural instability over less than 1 hr to a few days
3. Not responsive to Sinemet

# Progress

- Tested positive for DYT1 GAG946 deletion.
- Tried Sinemet without success.
- Tried Botox injections to the L shoulder without success.
- Responded somewhat to Klonopin.
- Waiting for DBS in the globus pallidus.
- Genetic testing for family members in Japan.

## Torsin A (TOR1A)

- Encodes for protein of unknown function.
- Structural similarity to the ATP-binding superfamily of chaperone-like proteins and AAA (ATPase associated with various cellular activities) superfamily important in vesicle fusion, neurotransmitter release, prion aggregation.
- AAA family members form a 6 member, homomeric ring structure, frequently with substrate proteins or nucleic acid “threaded” through the hole.
- GAG (glutamic acid) deletion is the only mutation found. Located in the carboxyl terminus. May be involved in the formation of the ring structure or in the interaction with partner proteins.
- Nearby imperfect 24 bp tandem repeat.
- Found in DA neurons (SNpc), LC, CB dentate n, Purkinje cells, thalamus, hippocampus, frontal cortex.
- Homologue TorsinB (70%) is located nearby and is not expressed in the brain.