‘She Has Changed …’

(Dementia Grand Round Symposium – Case Sharing)

3 NOV 2018
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TAI PO HOSPITAL
Lives with husband and son's family, retired garment factory worker

Education up to P.4

FU GOPD x DM, HT, hyperlipidemia
- Amlodipine 10mg daily
- Gliclazide 160mg bd
- Metformin 1g bd
- Vitamin B6 50mg daily

11/1/2017

“decline memory”

“refer OT for MMSE”
GOPD - 6.2.2017

- “bilateral visual floaters for 1-2 years”
- “progressive cognitive deterioration”
- “change of personality and behavior”
- “lost way home 6/12”
- “cannot use phone as before”
- “cannot take care of own self”

Refer AED for admission
“↓ memory, personality change, ADL pd”

GCS 15/15 PEARL, dull, ?deafness, power full, reflexes normal

VA: R 20/50 L 20/50

Blood x TSH, folate, TSH taken

CT brain – no ICH, no SOL

Home

Refer UMC 8/2/2017
Progressive ↓ memory, sometimes forgot daughter name, forgot the route to home
Remote memory mostly preserved
Low mood+
No focal neurological symptoms
Progressive ↓ hearing and ↓ vision for long time
folate 23.2, TSH/B12 pending
Refer memory clinic
Memory Clinic - 21.3.2017

- Progressive decline in memory in 2-3 years
- Relatively abrupt deterioration in recent half year
  - forgot his son name during worship, unable to recall the bus no. she was taking
- Difficulty in speech and writing
- Difficulty in expressing herself
- Unable to name objects
- Difficulty in finding way to daughter who lives in Kowloon
Memory Clinic - 21.3.2017

- BADL independent
- Not cope with taking care of grandson
- Decreased quality of cooking
Psychiatric symptoms

- Delusion
  - Theft: husband steals her money
  - Persecution: husband poisons her, relatives takes over her property in China
  - Jealousy: husband has EMA

- Anxiety

- Tearful when mentioning husband

- Distressed by relationship with husband, frequent argument
Cognitive test

- MoCA 7/30, <2\textsuperscript{nd} percentile of corresponding age and education
- executive function impaired
- sustained attention and working memory impaired
- serial 7: 1/5, starting subtracting 3, can't remember last answer
- immediate recall: 0/5, free recall: 0/5, recognition: 2/5
- sentence repetition: 1/2
- oriented to date, grossly oriented to hospital, but can't name hospital
- verbal fluency: poor, 4 items/minute
Physical examination

- Power full and symmetrical
- No limb rigidity
- No cerebellar signs
- Normal gait

CVS, chest, abdomen NAD
Other physical complaints

- Bilateral blurring of vision
  - Told to have astigmatism in eye check, improved with corrective glasses
  - Floaters persistent
  - Visual acuity grossly normal, no visual field loss

- Hearing impairment
  - Otoscopy: mild abrasion over EAC of right ear
Basic investigations

- CBC, LRFT N
- Vit B12, Folate, TSH N
- CT brain (2/2017): Patchy hypodense foci in bilateral corona radiata could be due to small vessel disease.
Differential diagnosis

- Dementia
  - Alzheimer’s
  - Vascular
  - Frontotemporal
- Depression
- Delusional disorder
Management

- Aspirin
- Refer psychiatry
- Refer ENT
- Refer eye
- MRI brain
Memory Clinic FU – 1.8.2017

- Nominal aphasia
- No articulation problem
- Could not remember names of children
- CT brain images reviewed
  - ?asymmetrical atrophy
Memory Clinic FU – 1.8.2017

- Nominal aphasia
- No articulation problem
- Cannot remember names of children
- CT brain images reviewed
  - asymmetrical atrophy
- ?PPA
- Book brain perfusion scan
- Pending MRI 10.2018
Memory Clinic - 21.11.2017

- Tearing during consultation, when saying how good her children were
- Expressed suicidal thoughts but no actual acts
- Tried sertraline 25mg daily
- Pending psychiatry appt.
Hospital admission 10-20.12.2017

- Unstable emotion
- Difficulty in naming and word finding
- Retained language skills in her mother language
- Spoke in alternating Cantonese to Mandarin even when other people talk to her in Cantonese
- Low mood because of cognitive decline
- Failed to recall how many children she has
- Refused to take sertraline as she did not believe it would help
Hospital admission 10-20.12.2017

- Hyponatremia 122, Osmo 256, Cr normal
- Urine Na <20, Osmo 185
- Started NaCl, TFT normal, am cortisol 314, Na improved to 134
- CT brain: no significant interval changes
Hospital admission 10-20.12.2017

- Seen by psychiatry:
  - ?frontotemporal dementia, daughter decided not for psychiatric admission
  - Start quetiapine 25mg nocte, stop sertraline
  - FU 4/52
Irritable when seeing husband and D-I-L

Dementia with BPSD (FTD Vs AD)

MSE:
- Kempt
- Euthymic, affect reactive
- Speech CR mostly, with word finding difficulty
- ? paranoid idea against her husband, she refused to elaborate and attempted to end the interview
- Denied AH/ VH
- Not suicidal/ violent
- Impaired insight

Donepezil 5mg nocte, keep quetiapine
Did not take quetiapine as patient felt she was not psychotic

Less irritable, jealousy similar
Severe hypoperfusion in left parietal, occipital and posterosuperior temporal region
Baseline Data vs. Elderly Normals III
Max Activity Comparison

Visuals Perfusion
Cortex 3D Volume Slices
Compare vs Population
Cortex 3D Volume Slices
Save Talarach Data
Save To Population
ECD perfusion SPECT
13.3.2018

- Specific severe hypoperfusion in the left posterior cortex involving left fronto-parietal speech pathway (logopenic PPA) and inferior longitudinal fasciculus (which is common speech pathway), pattern suggests logopenic PPA.

- Suggest clinical correlation.
Memory clinic FU – 20.3.2018

- Sometimes confused with the way to get home (2 staircases to reach home)
- Memory impairment static
- Refused to take donepezil and quetiapine
- Advised to resume
27.6.2018 - PSY FU

- Mood stable
- Refused to go out these few weeks
- Preoccupied by physical complaints yet could not express herself
- Word finding difficulty +ve
- MSE: kempt, euthymic, affect reactive, speech CR mostly, with word finding difficulty
- MoCA 13 <2\text{nd} percentile
- Resume donepezil, keep quetiapine, plan pregabalin if still anxious
Fear being burden to family
Fear getting lost and not want to go out
Unable to articulate any physical discomfort
Word finding difficulty
Not giving med by family, found manageable
Discussed with son: want to keep med-free
observation
Frontotemporal dementia

- Behavioral variant FTD (bvFTD)
- Primary progressive aphasia (PPA)
  - Nonfluent / agrammatic variant
  - Semantic variant
- Logopenic variant

Frontotemporal lobe degeneration (FTLD)

Alzheimer pathology
Clinicopathologic correlations of PPA

- Nonfluent / agrammatic - FTLD with tauopathy
- Semantic – FTLD with TDP-43 proteinopathy
- Logopenic - Alzheimer pathology, hemispheric asymmetry in the distribution of neurofibrillary tangles

PPA clinical syndrome is determined by anatomic predilection for the language network of the brain

Classification of primary progressive aphasia and its variants - American Academy of Neurology 2011

- Meet basic PPA criteria first
- Specific speech and language
- Imaging-supported
- Definite pathology

### Diagnostic criteria for primary progressive aphasia

**Inclusion: criteria 1–3 must be answered positively**

1. Most prominent clinical feature is difficulty with language
2. These deficits are the principal cause of impaired daily living activities
3. Aphasia should be the most prominent deficit at symptom onset and for the initial phases of the disease

**Exclusion: criteria 1–4 must be answered negatively**

1. Pattern of deficits is better accounted for by other nondegenerative nervous system or medical disorders
2. Cognitive disturbance is better accounted for by a psychiatric diagnosis
3. Prominent initial episodic memory, visual memory, and visuoperceptual impairments
4. Prominent, initial behavioral disturbance
### Diagnostic criteria for nonfluent/agrammatic variant PPA

1. **Clinical diagnosis of nonfluent/agrammatic variant PPA**
   - At least one of the following core features must be present:
     1. Agrammatism in language production
     2. Effortful, halting speech with inconsistent speech sound errors and distortions (uganda speech)
   - At least 2 of the following other features must be present:
     1. Impaired comprehension of syntactically complex sentences
     2. Spared single-word comprehension
     3. Spared object knowledge

### Diagnostic criteria for semantic variant PPA

1. **Clinical diagnosis of semantic variant PPA**
   - Both of the following core features must be present:
     1. Impaired confrontation naming
     2. Impaired single-word comprehension
   - At least 3 of the following other diagnostic features must be present:
     1. Impaired object knowledge, particularly for low-frequency or low familiarity items
     2. Surface dyslexia or dysgraphia
     3. Spared repetition
     4. Spared speech production (grammar and motor speech)

### Diagnostic criteria for logopenic variant PPA

1. **Clinical diagnosis of logopenic variant PPA**
   - Both of the following core features must be present:
     1. Impaired single-word retrieval in spontaneous speech and naming
     2. Impaired repetition of sentences and phrases
   - At least 3 of the following other features must be present:
     1. Speech (phonologic) errors in spontaneous speech and naming
     2. Spared single-word comprehension and object knowledge
     3. Spared motor speech
     4. Absence of frank agrammatism

### Imaging-supported nonfluent/agrammatic variant PPA diagnosis

- Clinical diagnosis of nonfluent/agrammatic variant PPA
- Imaging must show one or more of the following results:
  a. Predominant left posterior temporal atrophy on MRI
  b. Predominant left posterior parietal hypoperfusion or hypometabolism on SPECT or PET

### Nonfluent/agrammatic variant PPA with definite pathology

- Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
  1. Clinical diagnosis of nonfluent/agrammatic variant PPA
  2. Histopathologic evidence of a specific neurodegenerative pathol (e.g., FTLD-tau, FTLD-TDP, AD, other)
  3. Presence of a known pathogenic mutation

### Imaging-supported semantic variant PPA diagnosis

- Both of the following criteria must be present:
  1. Clinical diagnosis of semantic variant PPA
  2. Imaging must show one or more of the following results:
    a. Predominant anterior temporal atrophy
    b. Predominant anterior temporal hypoperfusion or hypometabolism on SPECT or PET

### Semantic variant PPA with definite pathology

- Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
  1. Clinical diagnosis of semantic variant PPA
  2. Histopathologic evidence of a specific neurodegenerative pathol (e.g., FTLD-tau, FTLD-TDP, AD, other)
  3. Presence of a known pathogenic mutation

### Imaging-supported diagnosis of logopenic variant PPA

- Both criteria must be present:
  1. Clinical diagnosis of logopenic variant PPA
  2. Imaging must show at least one of the following results:
    a. Predominant left posterior parietal hypoperfusion or hypometabolism on MRI
    b. Predominant left posterior parietal or parietal hypoperfusion or hypometabolism on SPECT or PET

### Logopenic variant PPA with definite pathology

- Clinical diagnosis (criterion 1 below) and either criterion 2 or 3 must be present:
  1. Clinical diagnosis of logopenic variant PPA
  2. Histopathologic evidence of a specific neurodegenerative pathol (e.g., AD, FTLD-tau, FTLD-TDP, other)
  3. Presence of a known pathogenic mutation
Treatment

- Non pharmacological

- Pharmacological

- No approved therapy

- Symptomatic management
  - Behavioural
  - Cognitive
  - Motor
Cholinesterase inhibitors

- No convincing evidence of benefit
- Unless there is diagnostic uncertainty and a diagnosis of Alzheimer disease seems equally as likely as FTD

Galantamine
- 36 FTD patients, 8-week randomized, double-blind, placebo-controlled withdrawal after 18 weeks treatment
- A trend toward benefit in global severity score in the PPA group, but not in bvFTD
- Language scores in treated PPA group remained stable compared to the placebo group, which showed deterioration

Donepezil

- Case series of 24 FTD patients over 6 months
- 4 patients in the treatment arm had worsening behavior
- donepezil-treated group had greater worsening on the FTD inventory
- Discontinuation of donepezil led to an abatement of behavioral symptoms

Cholinesterase inhibitors

- Rivastigmine
  - 20 patients, 12-month open-label study with 20 patients
  - some improvements in behavioral, depressive symptoms via the NPI score, but did not prevent cognitive deterioration as measured by MMSE

Thank you!