Clinical Features of Frontotemporal Dementia and Diffuse Lewy Body Dementia

Susan K. Schultz M.D.
University of Iowa Carver College of Medicine

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Variations in “Dementia” Syndromes

• Dementia versus Alzheimer’s Disease
• Alzheimer’s Disease, Vascular Disease
  – Most common dementias after age 65
  – Lewy Body Dementia – also often starts after age 65, has a unique course
• Frontotemporal Dementia
  – Starts earlier in life than the above
  – Both frontotemporal and Lewy body dementia do not have memory loss as a core feature.

Main Behavioral Characteristics of Frontotemporal Dementia

– Illustrated in case presentation
• Two Variants in Presentation
  – Disinhibited behaviors, repetitive questions
  • Loss of normal social engagement, expression
  • OR
  – Deterioration in language communication

Observations from Cases

• Burden of care
  – Younger onset than other dementias in the absence of medical frailty
  – Relatively “healthy” appearance can complicate caregiving
    • Delays accurate diagnosis
    • Problems in public places
    • Difficulty for facilities to manage care
    • Potential for harm: Driving, wandering, etc.

Case Presentation: Mrs. K

• Mrs. K is presently an 82-year-old Caucasian widowed female who resides in a long-term care facility
• Began having substantial changes in behavior in her late 60s, early 70s
  – Had no previous psychiatric history, enjoyed good physical and cognitive health throughout her life.
History of Present Illness

- At age 71 Mrs. K was living in an apartment (independently performing her ADLs, driving).
- She presented for “memory” evaluation
- Reported the following
  - Difficulty naming objects
  - Family told her she needed to clean her apartment
  - Observed to have “Shutter bug” behaviors
  - Took photos at odd times, photographed clinic staff
  - Appeared to compulsively carry one or more bottles of water at all times
- MMSE = 27/30

Medical History
- Polyps on colonoscopy
- Meds: aspirin, Metamucil, vitamin E 2000 units a day, calcium, multivitamin, and simethicone

Social History
- 12th grade education
- Worked in a clerical position
- Cigarettes: brief history in young adulthood
- No history of alcohol issues or illicit drug use

Family History
- Negative for dementia

Atrophy noted on MRI

Temporal atrophy

MRI Report
- Severe atrophy of the temporal lobes bilaterally, left > right
- Subtle frontal atrophy
- Mild dilatation of the lateral ventricles
- Marked dilatation of the ventral horns

Neuropsychological Testing

- Atypical dementia, characterized by deficits in expressive language and higher-order reasoning abilities, with a relative sparing of basic perceptual abilities and speed of processing. Results suggest early frontal dementia.
  - Comment: She offered vague responses to specific questions. She had good social skills, although on several occasions she laughed inappropriately when discussing her cognitive difficulties; insight seemed limited.

Two Years Later, Age 73

- Still living independently in an apartment
  - Hoarding behaviors – cluttered belongings left only narrow paths to move about her apartment
- Clinical Notes:
  - More dependent on family for financial decisions
  - Difficulty with making decisions at a restaurant
- Neuropsychological testing:
  - Continues to demonstrate impairments in the areas of language, and executive functions.
    - In contrast, orientation, visuospatial and visuoconstructual abilities appeared generally intact.
  - These results are consistent with frontotemporal dementia, with greater dysfunction of the language dominant hemisphere.
Four years later, Age 75

- Continues to decline in function and have progressive increase in disinhibition, poor judgment, and personality changes.
- Exam: Dressed somewhat bizarrely, in a purple T-shirt with purple leggings.
- Her hair was unkempt, and she clearly needed more assistance with grooming. Carrying three bags, a coat, and a camera.
- Obsessive about taking pictures, and would not let her purse out of her hands.

Neuropsychological Testing: Age 76

- Impairments in memory, significant decline in language abilities and executive functions.
- Prominent behavioral disinhibition (e.g., hugging and kissing the examiner following the assessment; giggling).
- Consistent with FTD, although older than normal profile.

Change in Dwelling: Age 76

- Transitioned to assisted living facility
- No longer driving
- After a short time in assisted living – wandered away in the neighborhood, found and brought back by family
- Right hip fracture, Age 77
  - Hospitalization for hip fracture
    - Sundowning behavior, attempting to get out of bed without assistance
    - Delusions, hallucinations, and aggression which prompted brief use of haloperidol 0.5 mg BID with good response

Nursing Home

- Repetitive questions
- Walking without walker
- Repeatedly getting up to the bathroom
- Multiple repetitive requests, demands, anxiety, and is very talkative
- Insomnia
- Several falls

Head CT post-falling
Notable for: Progressive atrophic change, hematoma

Current State: Age 81

Meds:
Tylenol, HCTZ, ECASA, Atenolol, Colace, levothyroxine, Miralax, sertraline 100 mg qd and trazodone 25 mg hs

Mental Status:
- Alert and smiles. Oriented to name only. Deficits in memory and cognition. Attention and concentration are good. Insight and judgment are poor. Mood is neutral with no suicidal ideation. She expresses no overt psychosis. No tremor, rigidity, or abnormal tongue movements. She tells me she loves me.
Frontotemporal Dementia (FTD)

- Distinct clinical variants of FTD
  - Behavioral-variant
  - Changes in behavior and personality.
    - Frontal-predominant cortical degeneration
  - Semantic dementia
    - Progressive loss of knowledge about words and objects.
    - Anterior temporal neuronal loss
  - Progressive non-fluent aphasia
    - Effortful language output, loss of grammar and motor speech deficits.
    - Left perisylvian cortical atrophy.

DIAGNOSIS: DSM-5 Frontotemporal Neurocognitive Disorder: Behavioral Variant

- Behavioral disinhibition: Socially inappropriate behavior; or loss of manners or decorum; or impulsive, rash, or careless actions. At least 3 of the following:
  - Apathy or inertia
  - Loss of sympathy or empathy
  - Diminished response to other people’s needs and feelings; diminished social interest, interrelatedness, or personal warmth
  - Perseverative, stereotyped, or compulsive/ritualistic behavior
  - Hyperorality and dietary changes

DSM-5 Frontotemporal Neurocognitive Disorder: Language Variant

- Both of the following must be present:
  - Gradual worsening of language function, in the form of speech production, word finding, object naming, grammar, or word comprehension; with evidence that language function was normal premorbidly.
  - Memory function and visuospatial skills are comparatively less impaired or not impaired relative to the language impairment which must be at least moderate.

FTD Neuropathology: From Pick’s to Ubiquitin to MAPT

- “Classical Pick’s disease”
  - Pick bodies: tau-positive round neuronal inclusions
- FTD-U
  - Mutations in progranulin gene, chromosome 17
  - Comprises the greatest number of FTD patients, may include a FTD-MND variant
- FTD-tau
  - Microtubule-associated protein tau (MAPT) gene, chromosome 17, includes FTD-P, with parkinsonism
  - Now ~60 MAPT mutations associated with FTD

Prognosis and Treatment

- The rate of progression varies.
  - Slowly progressive language dysfunction over 10-12 years, disinhibition may evolve to more apathy
- Medications?
  - Cholinesterase Inhibitors not beneficial (Mendez 2007)
  - Small trials of SSRIs, trazodone for sleep suggest modest benefit. (Moretti R, 2003)
- Treatment is about ENVIRONMENT, SAFETY and support to caregivers!
Lewy Body Disease

- Many similarities and overlap with the pathology of Parkinson’s disease
- Prominent cognitive impairments
  - Poor attention, SLOW information processing
  - Memory is relatively less impaired
- Propensity for adverse effects from medications and high risk for delirium

Dementia with Lewy Bodies

- Mean age at diagnosis = 75 years, males
- Lewy bodies contain alpha-synuclein
  - Aggregates in Diffuse Lewy Body Disease
  - Confluence of Parkinson’s disease motor symptoms with dementia features and vivid visual hallucinations
- Clinical Hallmark: Neuroleptic (Antipsychotic medication) sensitivity
  - Persons with Lewy Body disease who display severe reactions to antipsychotic medications have a higher mortality risk than those who do not.


Criteria for a Neurocognitive Disorder Due to Dementia with Lewy Bodies

- Core Diagnostic Features include:
  - Fluctuating cognition with pronounced variations in attention and alertness.
  - Recurrent visual hallucinations which are typically well-formed and detailed.
  - Spontaneous features of parkinsonism with onset at least 1 year later than the cognitive impairment.

Criteria: Suggestive Diagnostic Features of Lewy Body Dementia Include:

- REM sleep behavior disorder
  - Moving or speaking during REM sleep, also confusion between the dreaming state and waking state
- Severe neuroleptic sensitivity
  - Poor response to antipsychotic medications
  - Significant worsening of Parkinson’s symptoms

LBD: Management Issues

- Parkinsonism
  - Poorly responsive to dopaminergic medications
- Visual Hallucinations
  - Reassurance, not medications if there is no distress from visual symptoms
- Fluctuating Sensorium
  - Very high risk for delirium, impaired alertness
- Care Issues
  - Repeated falls, syncope, depression, episodic unconsciousness

Lewy Body Dementia: Strategies

- Minimize medications for Parkinson’s if possible
  - Hypophonia, rigidity (axial bias: truncal) but less tremor, more facial impassivity
  - Consider a cholinesterase inhibitor?
    - Data are not clear, careful re: side effects
- Use antidepressants carefully or avoid
- Avoid antipsychotic medications if at all possible
- Educate caregivers, allow time for responses
  - Remember that information processing is slow and attention may be impaired
- Work on environment, provide support
Summary

- “Dementia”
  - May vary in age of onset, course and features depending on the type
  - Understanding the less common types can be very helpful in providing optimal care
    - Communication can be improved if there is an awareness that there is slowed thinking in LBD or impaired language but preserved memory in FTD

- Thank you!