Frontotemporal Dementia (FTD)

Compare and contrast with Alzheimer disease

- Most common cause of dementia by far -70%
- More common with advancing age
  - ≥ 65 YO $\rightarrow$ 7 %
  - ≥ 85 YO $\rightarrow$ 30-47 %
- Insidious onset, slowly progressive course
- Earliest manifestation usually STM (short term memory loss)

- Other early cognitive deficits
  - Executive function (abstract thinking, planning, organizing)
  - Language (forget words, verbal expression, comprehension of reading)
- Middle-to-late stage manifestations
  - Gait instability / falls
  - Incontinence
  - BPSD (Behavioral and Psychological Symptoms of Dementia)
  - Personality changes
  - At best, modest / temporary improvement with CEI (cholinesterase inhibitors)

FTD

- Pathologically / clinically heterogeneous disorder with focal degeneration of frontal and/or temporal lobes
- Onset typically late 50's- early 60's; mean age 58
  - Onset 20-80; unusual < 40 or > 75
- Earliest manifestations
  - Personality changes / social behavior changes (behavior variant)
  - Language deficits
- Slowly progressive to more global dementia
- Some with extrapyramidal or motor symptoms
- 1/3 with FH

- Pick disease $\rightarrow$ behavioral variant with Pick bodies (intracellular inclusions)
- Other terms
  - Frontal lobe dementia
  - Frontal lobe degeneration
  - Frontotemporal lobar degeneration
  - Pick complex

FTD Subtypes

- Behavioral variant (BV)
- Progressive Nonfluent Aphasia (PNFA)
- Semantic Dementia (SD) $\rightarrow$ progressive fluent aphasia
- Motor Syndromes
    - Motor Neuron Disease (MND)
    - Corticobasilar Degeneration (CBD)
    - Progressive Supranuclear Palsy (PSP)

Clinical manifestations:

- Progressive Δ in personality / social behavior OR
- Progressive aphasia
- Ultimately a global dementia
- More rapid progression than AD; shorter with motor neuron variant
  - Four- eight years

Behavioral Variant

- Most common presentation of FTD
- Personality Δ
  - Apathy $\rightarrow$ withdrawal; $\downarrow$ spontaneity; abulia
  - Social disinhibition / impulsivity / $\uparrow$ sentimentality / violent aggression
- Lack insight
  - All by two years
  - Lack of concern
- Loss of social awareness
  - Offensive remarks; inappropriate behavior
  - Hygiene; inappropriate elimination
  - Antisocial acts; criminal acts
  - Inappropriate sexual comments; $\downarrow$ libido

- Stereotypical or ritual behaviors
  - Same foods
  - Catch-phrase
  - Hoarding
  - Counting
  - Pacing
- Eating pattern Δ's
  - overeat; binge
  - $\uparrow$ ETOH
  - Hyperorality
- Emotional blunting / loss of empathy
  - Self- centered
  - Difficulty recognizing others' emotional expression

- Mental rigidity
  - Inflexible routines
  - Inability to adapt to new situations
  - Inability to see others' point of view
- Deficits modulating attention
  - Distractibility
  - Perseverative behavior
  - Utilization behavior
- Collateral history is imperative

- Cognitive function relatively intact early (MMSE)
  - With progression → impaired executive function, problem-solving, attention
  - Memory and visuospatial skills less severe
- Subtype with impaired executive function and subtle behavioral Δ's initially
- Altered speech
  - Aspontaneity - echolalia
  - Paucity of speech - perseveration
  - ↑'d, often pressured, speech
  - Stereotypy - mutism

- Progressive Nonfluent Aphasia
  - Anomia is initial manifestation
    - Word-finding; object naming
  - Progressively dysfluent speech
    - simplification; circumlocution; phonemic paraphasia
  - Ultimately, difficulty with comprehension; may become mute
  - Restricted to expressive language for few- several; years global dementia later
  - Some develop behavioral manifestations or motor neuron disease
  - MRI – left perisylvian atrophy

Semantic Dementia (temporal variant)

- Initially a progressive speech disturbance
  - Impaired comprehension; anomia; semantic parapahasias
  - Normal fluency $\rightarrow$ effortless speech lacking meaning & information
  - Normal repetition
- Incomplete awareness, particularly impaired comprehension
- Dyslexia / dysgraphia
- Read and write phonetically
- Verbal fluency tests
  - category fluency $>$ letter fluency
- MRI- temporal atrophy, L $>$ R; more anteriorly than AD

- Visual object recognition impairment affects long-term memory
- Episodic memory (autobiographical) is relatively preserved
- Less commonly R temporal lobe deficits
  - recognizing faces / voices
- Behavioral problems usually within few years

Motor Syndromes

- Motor Neuron Disease (MND)
- Corticobasal Degeneration (CBD)
- Progressive Supranuclear Palsy (PSP)

Motor Neuron disease (MND)

- Precede or follow dementia, usually behavioral variant
- 50 % with MND have / develop dementia
- Progressive atrophy / flaccidity / fasciculation's of predominantly bulbar muscles and UE’s
- UMN signs less prominent
- Clinical features of both FTD-MND usually within two years
- Course more rapidly progressive
- MRI- bifrontal atrophy

Corticobasal degeneration (CBD)

- Asymmetric rigidity / apraxia
- Alien limb syndrome
- Dystonia
- Impaired joint position, 2-point discrimination, agraphesthesia
- Mirror movements
- Gait impairment and supranuclear gaze palsy spread to other side
- Cognitive impairment develops in most
- MRI- asymmetric atrophy of frontoparietal, basal ganglia and/or cerebral peduncles

Progressive Supranuclear Palsy (PSP)

- Supranuclear vertical gaze palsy
- Axial dystonia
- Bradykinesia
- Rigidity
- Falls
- Most with dementia and overlap with behavioral variant FTD
- MRI- symmetric atrophy of superior cerebellar peduncle and midbrain

Differential Dx

- Of BV – FTD
  - Psychiatric disorder → bipolar; OCD; depression
    - Major psychoses uncommon in BV-FTD (delusions, hallucinations)
  - AD
    - Younger onset; prominent behavioral sxs without significant amnesia
  - DLBD
    - Early visual hallucinations
  - Structural frontal lobe disease → MRI
    - CVA, tumor , abscess

BV-FTD (99% sensitive / 80-85% specific)

- Abnormal social conduct
- Eating disorders
- Stereotyped behavior
- Apathy
- Absent memory / visuospatial deficits

Differential Dx of progressive aphasia

- Most with progressive aphasia consistent with PNFA or SD have FTD at autopsy
- AD $\rightarrow$ 1/3 of PNFA or SD had AD
- VD
- Primary brain tumor $\rightarrow$ MRI
- DLBD $\rightarrow$ ~ 15 % with progressive aphasia have DLBD

- Neuropsychological testing for diagnosis is limited
- FTD > AD
  - ↓ performance on executive function and social cognition
  - ↑ performance on memory and visuospatial function

Treatment of FTD

- No FDA- approved tx
- Neurochemical basis for FTD is unknown
- Abnormalities in serotonin and dopamine
  - not cholinergic
- SSRI's
  - disinhibition; impulsivity; repetitive behavior; eating disorders; sexual disinhibition
- Trazodone
  - agitation; aggression; depression; eating disorder

Treatment of FTD

- Atypical antipsychotics (olanzapine, quetiapine, aripiprazole)
  - agitation
  - particularly vulnerable to EPS; use as last resort
  - quetiapine with less D2 antagonism
- Stimulants (Methylphenidate, dextroamphetamine)
  - ↑ DA & NE
  - apathy; disinhibition
  - may cause delirium