Overview of Frontotemporal Dementia

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Neurodegenerative disease

- A neurodegenerative disease = a brain illness that worsens over time

Dementia

- A neurodegenerative disease (brain illness that worsens over time)
- Affecting cognition (thinking/mental processes) and/or behavior
- Interferes with daily functioning
- Usually worsens gradually (over years)

Dr. Lipton's 5 A's of Dementia

- Amnesia (memory disorder)
- Abstract (problems with executive functioning)
- Agnosia (perceptual difficulty)
- Aphasia (language problem)
- Apraxia (motor problem)

FTD = Frontotemporal dementia

FTLD = Frontotemporal dementia

Frontal lobes control executive function
Temporal lobes: memory, language

Diagnostic Criteria

- Lund-Manchester Criteria (JNNP,1994)
- FTLD Consensus criteria (Neary et al., Neurology, Dec. 1998)
- FTD Workgroup (McKhann et al., Arch Neurol., Nov. 2001)

FTD variants

- Behavioral predominant (frontal/behavioral variant)
- Language predominant
  - Primary progressive aphasia
  - Semantic dementia
- Motor predominant
  - CBD
  - Progressive Supranuclear Palsy
  - Frontotemporal dementia-MND

Frontotemporal Dementia

- Neurobehavioral syndrome
  - Frontal variant (fv) or Behavioral variant (bv) of Frontotemporal Dementia (FTD)
  - fvFTD or bvFTD
- Language Presentation
  - Progressive nonfluent aphasia/Primary progressive aphasia (PPA)
  - Semantic Dementia (SD)/"temporal variant FTD"

FTLD Consensus Criteria

- Common features of FTLD
  - Gradual and insidious
  - Aphasia +/- agnosia
- Supportive features
  - Onset before 65
  - Positive family history
  - Motor Neuron Disease

FTD Behavioral Syndrome

- Apathy, social withdrawal +/- disinhibition
- Decreased executive function, poor self care
- Kluver-Bucy
  - hyperphagia, hypermetamorphosis, aggression +/- changes in sexuality
- Compulsions
- Perception, memory, praxis, and visuospatial skills relatively well preserved

Primary Progressive Aphasia

- Insidious onset and gradual progression
- Nonfluent spontaneous speech w/at least one of the following: agrammatism, phonemic paraphasias, anomia
- Other aspects of cognition are relatively well preserved

Semantic Dementia

- Semantic aphasia and associative agnosia
  - Insidious onset and gradual progression
  - Language +/- perceptual disorder
  - Other aspects of cognition, including memory, are relatively preserved
  - Preserved perceptual matching and drawing reproduction
  - Preserved single-word repetition, reading, taking dictation

Motor Neuron Disease

- MND
- Amyotrophic lateral sclerosis (ALS)
- Lou Gehrig's disease

- Frontotemporal dementia + MND = FTD-MND
- Either motor symptoms or cognitive/behavioral symptoms may come first

Motor neuron disease

- Weakness
  - Dysarthria (slurred speech)
  - Dysphagia (difficulty swallowing)
  - Limb weakness
- Changes in reflexes (hyporeflexia and hyperreflexia
- Muscle wasting/atrophy
- EMG/NCS

Frontotemporal dementia and Parkinsonism

- FTD-P
- Parkinson's-Plus Syndromes overlapping with Frontotemporal dementia
  - Corticobasal degeneration (CBD, formerly known as Corticobasal ganglionic degeneration/CBGD)
  - Progressive Supranuclear Palsy (PSP)

Parkinson's Disease

- 4 cardinal signs:
  - **T**remor (Rest tremor)
  - **R**igidity
  - **A**kinesia/bradykinesia
  - **P**ostural instability
- Clinical response to L-dopa
- Asymmetry

Progressive Supranuclear Palsy

- Bradykinesia
- Axial parkinsonism
- Postural instability
- Impairment of ocular gaze, first down
- Dysarthria
- Dysphagia
- Nuchal rigidity
- Psychiatric symptoms - labile affect, dementia

Corticobasal degeneration

- Hemiparkinsonism
- Apraxia
- "Alien limb" syndrome

Cognitive domains affected in PSP/CBD

- Motor AND cognitive deficits
- Apraxia
- IQ
- Executive function
- Visuospatial
- Attention
- Memory

Behavioral symptoms in CBD/PSP

- Apathy
- Disinhibition
- Orbitofrontal and medial frontal circuits

Psychiatric symptoms in CBD/PSP

- Depression
- Anxiety
- Sleep disturbance
- Usually not psychosis (hallucinations/delusions)

Diagnostic Evaluation

- Interview with patient and family
- Neurological evaluation
- Neuropsychological evaluation
- Neuroimaging
- Laboratory evaluation
- Additional tests may include: lumbar puncture/LP (spinal tap), speech-language evaluation, EMG/NCS

Neurological Examination

- Frontal reflexes
- Motor neuron signs
  - Weakness, fasciculations (twitching), etc.
- Parkinsonism
- Apraxia
- Alien limb syndrome

Treatment – Cognitive Enhancers

- Memantine (Namenda)
  - Possible neuroprotective effect
  - May benefit cognition, behavior, communication, and daily and motor function
- Cholinesterase Inhibitors
  - No cholinergic deficit
  - No effect, bad effect (increase irritability), or ?help - low doses

Treatment – Other Cognitive Strategies

- Daily routine/weekly schedule
- Structured activities/Brain Therapy
  - Social
  - Mental
  - Physical
  - Spiritual

Treatment of Aphasia

- Dopaminergic agonists
- Carbidopa-Levodopa (Sinemet)
- Memantine
- Speech-Language Therapy
- Sign/gestural/language
- Communication boards/books
- Writing
- Singing
- Art therapy

Treatment – Mood/behavioral symptoms

- Selective serotonin reuptake inhibitors (SSRIs)
  - Profound presynaptic serotonergic dficit (Sparks and Markesbery, 1991)
  - May help apathy/depression/mood swings, attention, irritability, impulsivity, and compulsions
- Sertraline (Zoloft)/Lexapro (escitalopram)
  - perhaps due to propensity for 5HT *and* dopamine uptake blockade
  - animal models show decreased 5HT/dopamine/HVA in frontal lobes
  - Relatively "neutral", i.e., help apathy, but don't worsen irritability

Treatment – Mood/behavioral symptoms

- Paxil (paroxetine)
  - Used by a number of specialists
  - More anticholinergic, so may worsen memory
  - Also may worsen irritability
- Prozac (fluoxetine)
  - Not favored/see above issues with paroxetine
- Selective serotonin and norepinephrine reuptake inhibitors: venlafaxine (Effexor) and Cymbalta (duloxetine)
  - May worsen irritability due to norepeinephrine effects

Treatment – Behavioral symptoms

- Agitation/aggression/psychosis/insomnia
  - Often respond to trazodone, SSRIs
  - If something stronger is necessary, prefer atypical antipsychotics (esp. quetiapine)
    - May try Geodon (ziprasidone), if weight gain is significant concern
    - Black box warning

Treatment – Behavioral symptoms

- Trazodone
  - One of few medications show to be effective in good scientific study (double-blind placebo-control trial)
  - Helped agitation/aggression, abnormal motor behavior (e.g., pacing), and overeating
  - Also has antidepressant effects
  - Initial dose ~25-50 mg (smallest tab = 50 mg, so 25 mg = ½ of a 50 mg tab)
  - May need to titrate up to 100-150 mg for insomnia
  - Side effects include sedation, dry mouth, dizziness, and priapism

Behavioral and Environmental Management

General approach to problem behavior

- Identify the problem behavior (WHAT?)
- Timing/frequency of the behavior (WHEN?)
- Surroundings/environment (WHERE?)
- Others involved? (WHO?)

General approach to problem behavior

- Very troubling / dangerous? (WHY?)
- Evaluation: physical & cognitive status
- Recommendations (WHAT TO DO?)

Behavioral Management Keys

- General environmental assessment
  - Nutrition and hydration
  - Acute and/or chronic illness
  - Sleep/wake cycle
  - Vision/hearing
- Target specific problem behaviors
  - Minimize use of medications
  - "Hugs not drugs"

Psychosis (Hallucinations and Delusions)

Don't argue, Don't confront, Don't deny
Give honest, non-committal answers
Understanding, patient explanations
Remain visible and available
Focus on familiar aspects of situation: voice, endearments, favorite things
Optimize sensory input: Lighting, glasses & hearing aids
Cooperate in search for mislaid Items

Pacing/wandering

- Wandering
  - ID bracelet, GPS
  - Manage environmental cues
  - Maximize familiarity, reassure
  - Distract with activity tasks, exercise
  - GO WITH PATIENT!
- Pacing/shadowing
  - Keep cool, private time, headphones
  - Distract with activity tasks

Principles of Environmental Management

- Serenity
  - Avoid overstimulation, behavioral triggers
  - Simplify communication, give cues
- Safety
  - Driving, Rx, guns, wandering, etc.
- Structure
  - Calm and routine environment
- Sanity
  - sheltered freedom

Simplicity

- Modify task and/or environment
- Remove clutter
- One thing at a time, one step at a time
- Emphasize routine, minimize change

Simply Communicate

- Speak slowly, simply, and directly (short sentences, one question at a time)
- Calm and positive manner and tone
- Face-to-face
- Address by name
- Demonstrate
- Fill in
- Don't expect a quick response

Treatment - Behavioral and Enviromental management

- Apathy – structure, routine, socialization
- Anxiety – distraction, redirection, support/reassurance
- Disinhibition – distraction, redirection, show don't tell, and don't show!
- Irritability/agitation – change subject, distraction, redirection

Conclusions

- FTD is not rare
- FTD can be differentiated from other dementias
- Subtypes of FTD can be diagnosed
- FTD can be treated
- Treatment of FTD varies according to subtype and symptoms
- Caregivers are the best treatment
  - Don't forget to stop and smell (or paint or pick) the roses!

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