Dementias other than Alzheimer’s Disease

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Dementia

Reduced mental skills impacting daily living, manifested by changes in:

• Memory
• Behavior
• Language
• Understanding (executive functioning)
• Emotions
Three stories:

• “The baby is inside”
• Doctor goes to high school reunion
• Mayor of small town
Where is the Pathology?

- **Language (parietal lobe)**
- **Intelligence, judgment, and behavior (frontal lobe)**
- **Memory (temporal lobe)**
What Kind of Insult?

Slow Process

Quick Event
How to Make a Diagnosis

• Clinical observation

• Genetic Biomarkers

• Protein Biomarkers

• Neuroanatomy
Conundrum

• High degree of overlap in presenting symptoms
• Compelling reason to identify specific diagnosis
• < 10 % cases reversed
Types of Dementia

- Frontotemporal Dementia - FTD
- Vascular Dementia
- Dementia with Lewy bodies
- Other dementias: alcoholic, CJD, others
Frontotemporal Lobar Degeneration
FTD diagnostic features

• Second most common variant, age < 65 years old
• Mean age 60 years old
• Survival 2 – 8 years
• Genetic in 40% of familial cases
• Common protein pathology with other dementias (Corticobasal degeneration, PSP, ALS, MND) (TDP-43 protein, FUS inclusions)
Progressive Non-fluent Aphasia

Slow, Effortful speech, Stuttering, Misuse of grammar, Verbs>Nouns, Eventual mutism
Semantic Dementia

Fluent but empty speech, Over-learned phrases, Loss of object identity, naming impairment, Loss of empathy
Behavioral Variant

Decline in social conduct, inappropriate remarks, risk taking, impulsive, loss of insight, emotional blunting, poor personal hygiene, compulsive use of instruments, poor attention and control, commonly misdiagnosed as depression or mental illness
Biology of FTD

• Mutation of an arm of chromosome 17 causing disruption of gene progranulin–
• Aggregation of Tau, Ubiquitin proteins ultimately destroying neuron.
• PNFA - Tau pathology
• Semantic - Ubiquitin pathology
• Behavioral - both
What can we do?

• No cure, treatment for symptoms
• **SSRI** beneficial for disinhibition, depression, repetitive behaviors
• **Antipsychotics** for aggressive, impulsive behaviors
• Caregiver needs, Support groups, Counseling
• Focus on functional needs, Social stressors, Behavioral management, Coordination of care,
• FTD Association
Dementia with Lewy Bodies
Lewy Body
Spectrum of Lewy Body diseases

• Dementia with Lewy Bodies (DLB) and Parkinson’s Disease with Dementia (PDD)

• Similar genetic and environmental risk factors: Pesticide exposure, High soil manganese, Synthetic heroin, Neuroleptics

• Both dopamine and choline deficits

• Aggregation of alpha-synuclein protein = lewy body
Symptoms

• Both cognitive and motor symptoms

• Executive, visual-spatial deficits, Hallucinations, Delusion, Agitation, Memory preserved early on.

• Dramatic fluctuations within the course of a day, Fatigue and agitation

• Falls common, Autonomic dysfunction (Hypotention, Incontinence), Dizziness,

• Brady-Kinesia, Rigidity, Postural Instability, REM sleep disorder
Useful Tests

• Frontal executive and visual-spatial deficits
  – Clock Drawing Test

• Diagnostic test: SPECT (dopamine binding)

• CSF analysis for tau and amyloid (normal tau, low amyloid)
Vascular Dementia
Vascular Dementia

- Multi-infarct or stroke related
- Risk factors: HTN, Smoking, DM, CAD, AFIB
- By the time the disease manifests, modifying risk factors may be too late
- Aneurysm, cerebral hypoxemia, genetic vascular disease also vascular related
- Lesions occur throughout brain - many manifestations
Vascular Dementia

• **Cortical** - primary damage in the cortex. Memory, language, thinking, and behavior

• **Subcortical** – Below the cortex, emotions, movement, memory
Common symptoms

- Memory impairment, language disorder, motor weakness, gait abnormality, pseudobulbar palsy (emotional lability)
- Most common: psychomotor slowing, attention deficits, executive dysfunction
- Stepwise deterioration
CADASIL

• Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy
  Small artery disease - newly described  mean age 45

• Sx: migraine with aura, subcortical ischemic events, mood disorder, apathy

• NOTCH 3 gene on Chromosome 19 (AD) got gene, got disease

• Pathologic hallmark: granules in media of arterioles (seen on skin biopsy)

• Genetic testing: ethical issues
Rapidly Progressive Dementias

- Creutzfeldt Jacob Disease - Mad Cow Disease
- Limbic and Hashimoto encephalopathy
- Infectious, autoimmune, paraneoplastic
Creutzfeldt Jacob Disease - Mad Cow Disease
Creutzfeldt Jacob

- Prion protein  5-12 month course
- 50-70 y/o
- Gravest prognosis in neurology “The great mimicker”
  - Cortical  – cognitive
  - Cerebellar  – motor
  - Extrapyramidal – behavioral and movement (tremor, myoclonus, dystonia)
- Characteristic EEG, myoclonus, pulvinar sign on MRI
Limbic Encephalitis

• Inflammatory encephalitis caused by antibodies reacting against a tumor - most common is the anti-Hu associated with small cell lung cancer, can cause memory loss, panic attacks, cerebellar degeneration, vertical gaze palsy, limb rigidity, dystonia, narcolepsy, REM sleep disorder
Hashimoto’s encephalopathy

- Abnormal high levels of thyroid antibodies
- Often have other autoimmune diseases such as diabetes, lupus, Sjogren
- Tremor, ataxia, hallucinations, stroke-like episodes, confusion, mood and behavioral disorder
- MRI findings are non-specific, generalized atrophy, cortical and subcortical changes
Other Causes

- **Infectious causes** – syphilis, lyme disease, HIV associated dementia, Whipples

- **Toxic/ metabolic** – Vit B12, Thiamine, niacin, folate deficiencies, uremic encephalopathy, hepatic encephalopathy, heavy metals (bismuth, lithium, mercury, arsenic, lead)

- **Autoimmune** - paraneoplastic limbic encephalitis, hashimoto encephalopathy, lupus cerebritis, sarcoid
Wernicke-Korsakoff

• “Let granny have her drink”
  – Frontal lobe greatest impact: poor judgement, difficulty with decisions, lack insight

• Also have memory and motor symptoms

• TX - replace thiamine
Diabetes and Dementia

- Insulin induced hypoglycemia - rapid cognitive changes
- Chronic hyperglycemia - cerebral microvascular disease
- Type 2 DM has a 1.5-2.5 fold increase risk of dementia
- Central pontine myelinolysis (osmotic demyelination) – rapid correction of low sodium – “locked in syndrome”
Prevention

• Causal disease prevention (stroke, blood pressure, alcoholism, head injury, HIV/AIDS)

• Early detection
Planning

- Caregiver support
- End of Life Issues
Chocolate Anyone???

Chocolate bars stacked on top of each other.


