Diseases Causing Dementia, Masquerading Conditions and Red Flags

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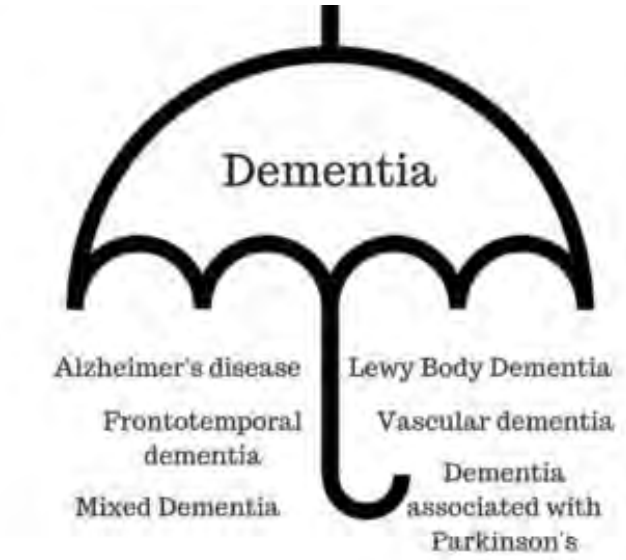
Learning Objectives

At the conclusion of this presentation, the participant will provide better patient care through an increased ability to:

- Describe major clinical features of the most common causes of dementia
- Recognize sensory, medical, and psychiatric conditions that may affect cognition and assessment of cognition
- Identify atypical clinical features which may warrant further investigation
- Consider genetic counseling for certain dementia subtypes
- Appreciate diagnostic imaging findings for certain dementia subtypes

Dementia

- Acquired, significant decline in 1(+) cognitive domain
  - Subjective appraisal or observation
  - Objective findings
- Impairments affect independence in daily functioning
- Not due to other conditions
  - Medical problems
  - Delirium
  - Psychosis
  - Substances



Masquerading Conditions / Rule Outs

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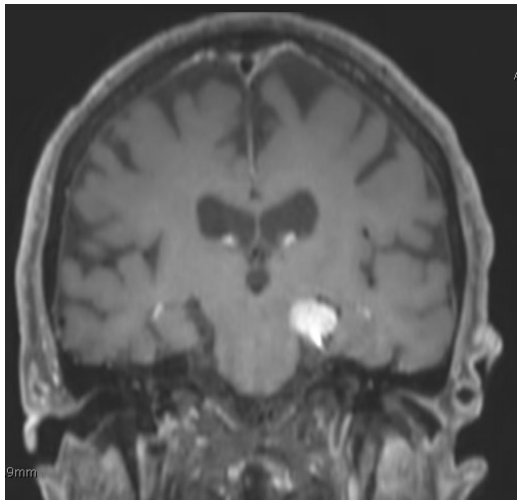
- Hearing loss, vision loss, primary language, formal education
  - Assess; have a voice amplifier and readers available; in person interpreter if possible
- Metabolic
  - CMP, CBC, vitamin B12, thyroid function; possibly HgA1c
- Medication side effects / Polypharmacy
  - Anticholinergic
    - oxybutynin; scopolamine; cyclobenzaprine; tricyclic antidepressants
    - OTC: diphenhydramine, doxylamine
  - Narcotics, opiates
  - Sleep medications
  - Benzodiazepines
- Delirium

Masquerading Conditions / Rule Outs

- Obstructive sleep apnea (OSA)
- Alcohol, marijuana, other drugs
- Depression, anxiety
- Other neurological conditions
  - Normal Pressure Hydrocephalus (NPH)
  - Seizure disorder
  - Brain tumor



Dementia, Delirium & Depression

Features	Dementia	Delirium	Depression
Memory problems	Yes (storage and recall)	Yes (storage and recall)	Yes (recall)
Onset	Gradual	Acute	Gradual
Mood disturbance	Possible	Possible	Yes
Disorientation	Possible	Yes	No
Sleep disturbance	Possible	Yes	Yes
Fluctuating symptoms throughout day	Yes	Yes	No
Progression	Gradual	Fast	Either
Somatic complaints	Possible	No	Yes
Apathy or anhedonia	Yes	Yes	Possible

Adapted from Downing et al, *Curr Psych Rev* 2013

Dementia Diagnostic Assessment

- Interview patient and close family/friend
- Vitals: blood pressure, heart rate, O2 sat; weight
- Brief neurologic examination (tone, gait)
- Cognitive testing (consider writing sample)

- Brain imaging
  - Structural: noncontrast MRI, ideally with coronal orientation; SWI sequence; 3T magnet
  - Functional: FDG-PET
- Neuropsychological assessment
- Molecular diagnostics
  - lumbar puncture
  - amyloid PET scan

Alzheimer's Disease

- Most common cause of dementia >65yo
- Females > males
- Roughly 7-10 year symptom time course

- Cardinal features
  - Insidious onset, gradual decline
  - Short term memory issues (episodic memory), word finding problems, difficulties with problem solving and reasoning
  - Procedural memory typically relatively preserved through mild stage

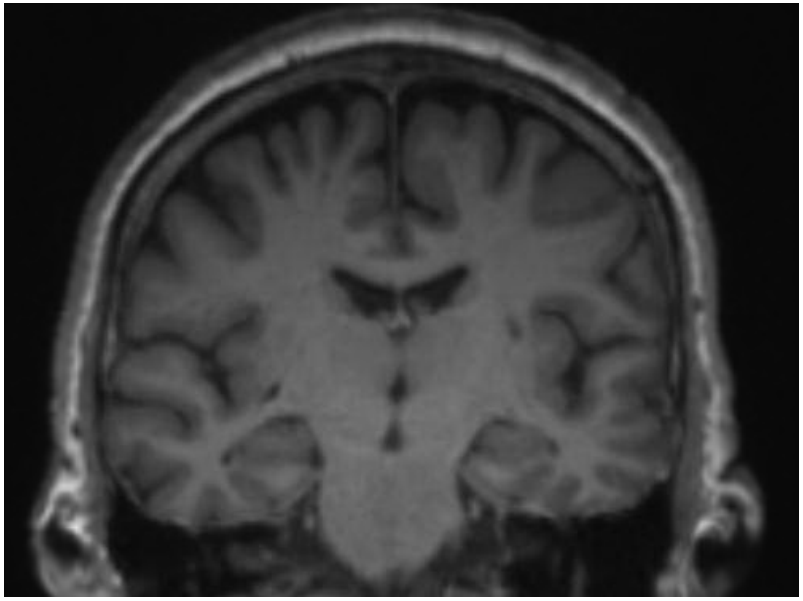
Alzheimer's Disease: Genetics

- "early onset" <65yo
  - Typically more rapid progression, and often non-amnestic presentation
  - May consider genetic testing for autosomal dominant gene variants, but typically low yield (<1% of AD)
  - Strongly recommend genetic counseling before performing testing

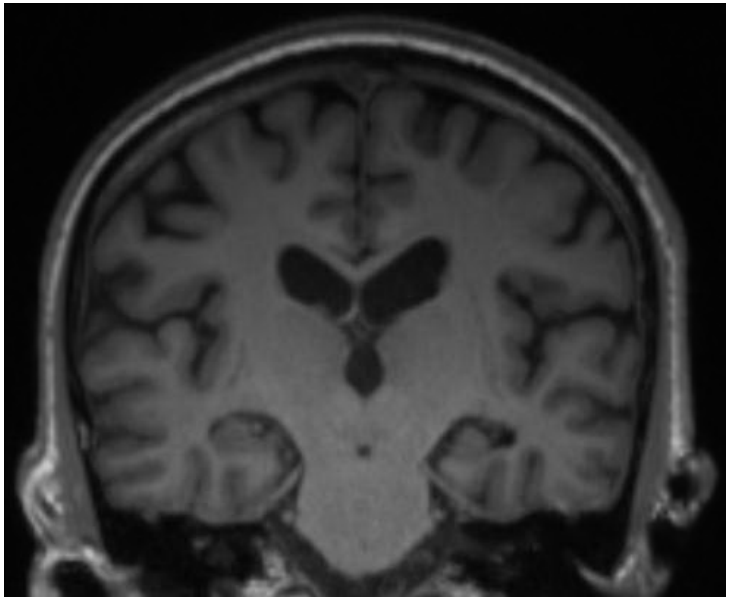
- Apolipoprotein E: ***risk*** allele for late onset AD
  - ApoE ε2 / ε3 / ε4
  - 1-2 copies of ε4 increases risk of developing late onset AD, but is not deterministic, and varies by population
  - Risk assessment before anti-amyloid mAb treatment

Alzheimer's Disease: Imaging

70 year old person
with normal hippocampal volume



69 year old person
with hippocampal atrophy



But you can't diagnose someone with dementia just by looking at a brain scan

Vascular Dementia

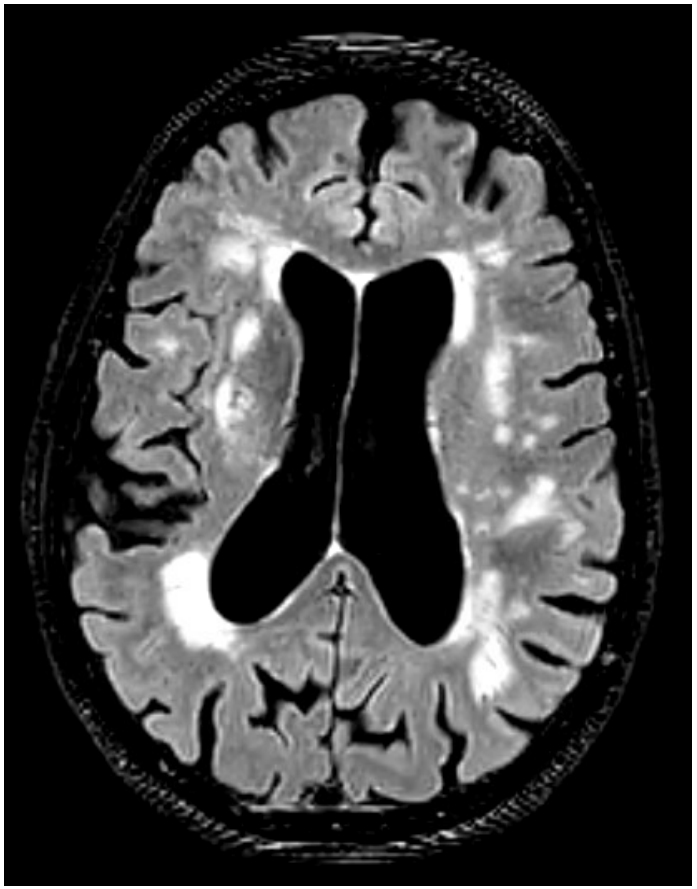
- Second most common cause of dementia
- Risk factors: diabetes, cigarette smoking, CAD, htn, dyslipidemia, afib, etc
- Subtypes
  - Ischemic versus hemorrhagic
  - Large versus small vessel disease
  - Cerebral amyloid angiopathy (CAA)

Vascular Dementia

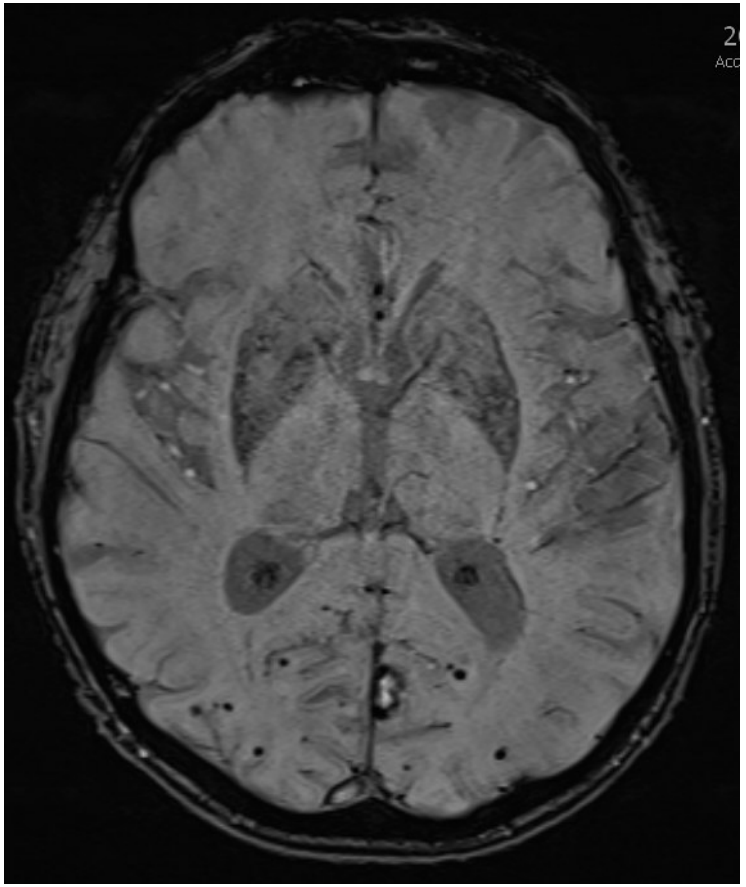
- Clinical presentation: “subcortical” pattern
  - Reduced processing speed / working memory / executive functioning
  - Retrieval can be improved via prompting
  - Apathy, depression, emotional blunting, bradyphrenia

Vascular Dementia: Imaging

Small vessel cerebrovascular disease



Cerebral Amyloid Angiopathy (CAA)



Lewy Body Disease

- Second most common neurodegenerative dementia
- Roughly 8-10 year symptom time course
- LBD is an umbrella term for
  - Dementia with Lewy Bodies (DLB)
    - Starts with cognitive changes
  - Parkinson's Disease Dementia (PDD)
    - Starts with movement changes
- Males >> females

Lewy Body Disease

- Core features
  - Visual hallucinations
  - Pronounced fluctuations in level of alertness
  - Parkinsonism
  - Cognitive testing: memory, attention, visuospatial skills

- Additional prominent features
  - REM sleep behavior disorder
  - Autonomic dysfunction
  - Extreme sensitivity to some antipsychotic medications

Frontotemporal Dementia

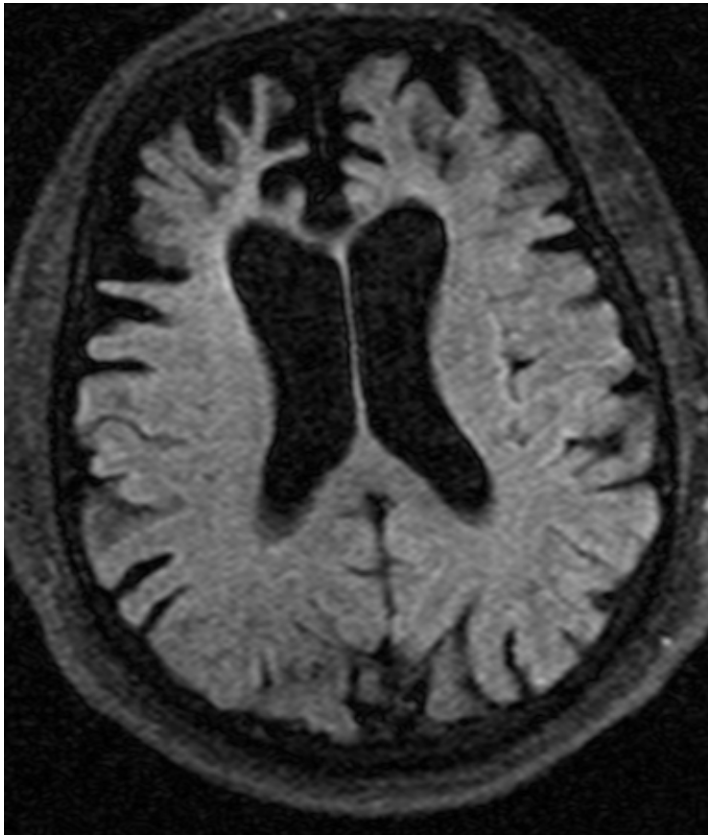
- Third most common neurodegenerative dementia
- Most common cause of early onset dementia
- Roughly 7-10 year symptom time course
  - But varies by subtype

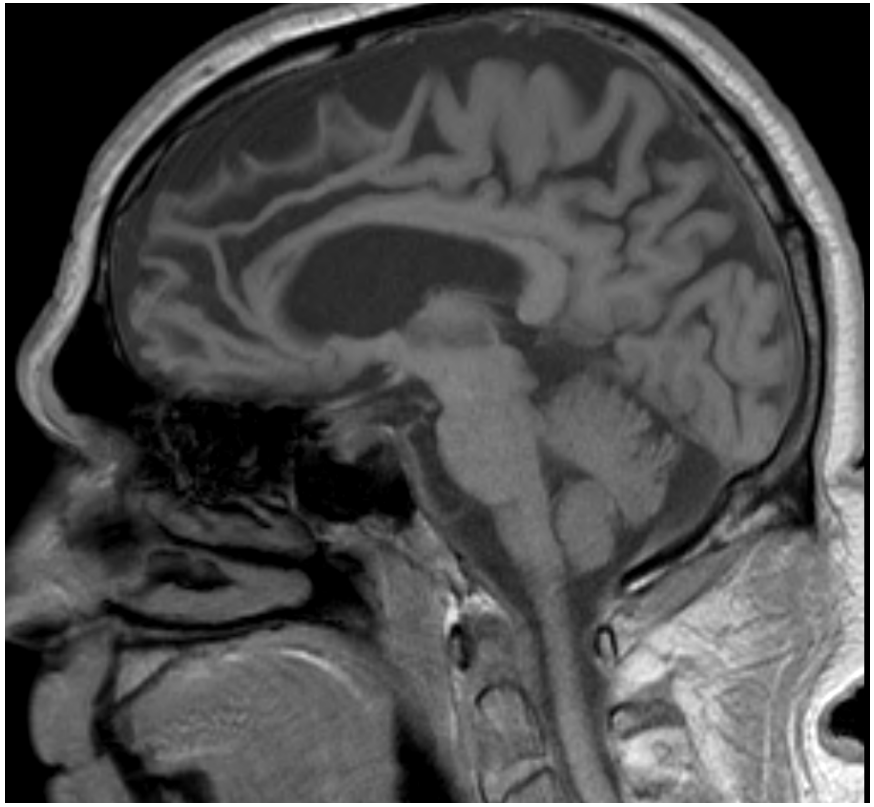
- ~30% monogenetic
  - *MAPT*, *GRN*, *C9orf72*
  - *C9orf72* also associated with motor neuron disease
  - Very strongly recommend genetic counseling before performing testing

Frontotemporal Dementia

- Behavioral variant (bvFTD)
  - Disinhibition, apathy, loss of sympathy / empathy, repetitive / compulsive behavior, dietary changes
- Language variants (Primary Progressive Aphasia)
  - Nonfluent variant PPA (nfvPPA)
    - Difficulty with motor speech planning
  - Semantic variant PPA (svPPA)
    - Difficulty with word knowledge

FTD: Imaging





Dementia: Summary of Common Etiologies

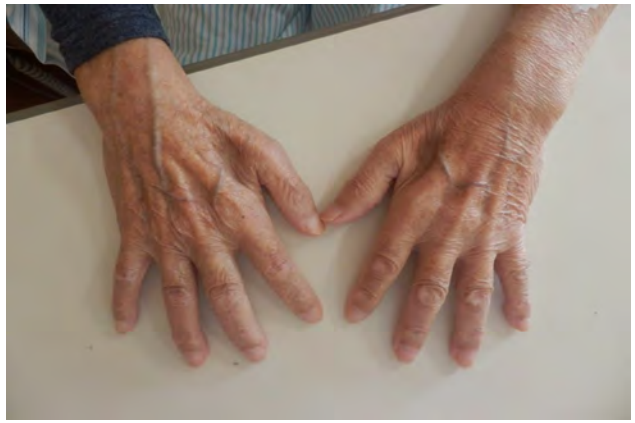
	Alzheimer's Disease	Vascular Dementia	Dementia with Lewy bodies	Frontotemporal Dementia
Prevalence	60–80%	15-30%	12-20%	10-15%
Early Symptoms	Memory loss Executive dysfunction Apathy/Depression Poor insight	Slow processing speed Poor attention Less memory impairment Poor acquisition/learning Apathy/Depression	Visual hallucinations Parkinsonism REM sleep behavior disorder Fluctuating cognition Visuospatial problems Memory loss	Behavioral issues Personality change Language problems Attention problems Executive dysfunction Poor insight
Cortical Changes	Temporal (medial) Parietal Frontal	Cortical Subcortical Lesion-specific	Occipital	Frontal Temporal (anterior)
Course	Progressive, gradual	Progressive, gradual or stepwise	Progressive, fluctuations	Progressive, faster decline
Associated Neuropathology	Beta-amyloid (plaques) *and* Tau (tangles)	Microvascular ischemic Hemorrhagic infarct Ischemic infarct Cerebral amyloid angiopathy	Alpha-synuclein (Lewy bodies)	Tau TDP-43

Adapted from K Rhoads ECHO presentation Jan 2022

Red Flags

Red Flags → More Extensive Workup

- Early onset (<60yo)
- Atypical onset / course
  - Non-memory symptoms (visual, language); rapidly progressive; fluctuations
- Unusual, early neurological symptoms
  - Tremor, gait changes, coordination issues, falls
  - Significant muscle atrophy, voice change (nasal or low volume), dysphagia
  - Urinary incontinence
- Early neuropsychiatric symptoms
  - Hallucinations
  - Delusions
  - Behavioral / personality changes



Komata, *J of Gen and Family Med*, 2018

Resources & References

- Pocketalker®
  - https://williamsav.com/pocketalker-personal-amplifier/
- 2023 AGS Beers Criteria®
  - https://agsjournals.onlinelibrary.wiley.com/doi/full/10.1111/jgs.18372
- STOP-BANG
  - Chung F, Abdullah HR, Liao P. STOP-Bang Questionnaire: A Practical Approach to Screen for Obstructive Sleep Apnea. *Chest* 2016;149(3):631-8.
- Epworth Sleepiness Scale
  - https://epworthsleepinessscale.com/about-the-ess/
- Alcohol Use Disorders Identification Test (AUDIT)
  - https://auditscreen.org/
- Patient Health Questionnaire depression module (PHQ-2/PHQ-9)
  - Kroenke K, Spitzer RL, Williams JB. The Patient Health Questionnaire-2: validity of a two-item depression screener. *Med Care* 2003;41(11):1284-92.
  - Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001;16:606–613.
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  - Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. *Clin Gerontol* 1986;5:165-173
- Generalized Anxiety Disorder (GAD-7)
  - Spitzer RL, Kroenke K, Williams JBW, Löwe B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Arch Intern Med* 2006;166(10):1092–1097.
- Geriatric Anxiety Inventory – Short Form (GAI-SF)
  - Byrne GJ, Pachana NA. Development and validation of a short form of the Geriatric Anxiety Inventory--the GAI-SF. *Int Psychogeriatr* 2011;23(1):125-31.

Resources & References

- Alzheimer's Association
  - www.alz.org (including 2023 AD Facts and Figures)
- American Stroke Association
  - www.stroke.org
- Cerebral Amyloid Angiopathy
  - angiopathy.org/introcaa
- Lewy Body Association
  - www.lbda.org
- Association for Frontotemporal Degeneration
  - www.theaftd.org
- FTD Talk
  - www.ftdtalk.org