Feb 21st, 5:10 PM - 5:40 PM

Diagnosis, Evaluation and Treatments for Dementia

John W. Margraf MD
Lehigh Valley Health Network, john.margraf@lvhn.org

Follow this and additional works at: http://scholarlyworks.lvhn.org/neurology_update_non_neurologist
Part of the Diagnosis Commons, Nervous System Diseases Commons, Neurology Commons, and the Neurosciences Commons


This Presentation is brought to you for free and open access by the Conferences and Symposia Collection at LVHN Scholarly Works. It has been accepted for inclusion in Neurology Update for the Non-Neurologist by an authorized administrator of LVHN Scholarly Works. For more information, please contact LibraryServices@lvhn.org.
Diagnosis, Evaluation and Treatment for Dementia

John Margraf, MD
75 y.o. female

- 3 year hx progressive short term memory loss
- 2 years ago stopped driving after she became lost
- Past 1-2 years speech punctuated by pauses to find proper word or substituting inappropriate word
- Past 1-2 years inability to attach names to familiar faces
- Past 6-12 months difficulty planning and preparing her own meals and eating mostly sweets and ice cream
- Gait slowing and shuffling more recently
- Increasing paranoia
Dementia

- Decline in cognition severe enough to interfere with daily life (social, occupational, etc.)
- Represents a decline from previous level of function
- No underlying systemic medical cause
Alzheimer’s Facts

- Affects 5 million in U.S; 17 million worldwide.
- Affects > 30% of persons > 80 y.o.
- 6th leading cause of death in this country and the only disease among the 10th deadliest that cannot be prevented, slowed, or cured.
- By the year 2050 estimated to affect 13.5 million people in U.S.
- Accounts for 50% of cases of dementia in autopsy and clinical series.
- Occurs naturally only in humans.
Genetics

- 1\textsuperscript{st} degree relative of a subject with late onset AD has 2x the expected risk of acquiring the disease.

- Concordance rate in twin studies (Swedish registry):
  - 59% for monozygotic twins
  - 35% for same sex dizygotic twins
  - 24% for opposite sex dizygotic twins
AD is pathologically characterized by the presence of extracellular amyloid plaques (composed of aggregated amyloid-β peptide) and intracellular neurofibrillary tangles (composed of aggregated tau).
Typical AD

- Memory loss is first and predominant complaint
- Associated with a deficit in at least 1 other cognitive domain
- Absence of early motor features
Core Elements of Declining Cognition (Domains)

- Memory – misplaces things, repeats, forgets conversations and appointments
- Speech – expressive speech +/- or comprehension
- Behavior and personality (apathetic, disinhibited, argumentative, compulsive, paranoid)
- Visuospatial – gets lost, difficulty dressing, hallucinations
- Executive – inability to make decisions, solve problems, complete complex tasks, handle gadgets
Mild Cognitive Impairment

- Concern regarding a decline in cognition not severe enough to impact independent living
- Often in one cognitive domain only and usually affecting memory (primarily short term)
- Conversion to dementia in 10-15% / year
- MMSE 25-27
Mild AD

- Decline in 2 or more domains
- Still able to care for self
- Decreased attention
- Difficulty with complex tasks
- Work trouble
- Halting speech
- MMSE 19-24
- Problems at work
Moderate AD

- Worsening memory, confusion, disorientation
- Appearance of behavioral symptoms, wandering, restlessness
- Increasing aphasia
- More difficulty with ADLs
- Unable to be left alone
- MMSE 10-18
Advanced AD

- Total dependency for ADLs
- Worsening behavior and gait progressing to bed and wheelchair existence
Subtypes of Alzheimer’s Disease

- Typical
- Hippocampal sparing
- Hippocampal predominant
- Clinical sx and patterns of atrophy on MRI parallel density and distribution of NFTs
Dementia - Etiologies

- Alzheimer’s disease
- Vascular Dementia
- Fronto-Temporal Lobar Dementia
- Lewy Body Disease
- Normal Pressure Hydrocephalus
- Others
Dementia: role of MRI updated version
Frederik Barkhof, Marieke Hazewinkel, Maja Binnewijzend and Robin Smithuis
Alzheimer Centre and Image Analysis Centre, Vrije Universiteit Medical Center, Amsterdam and the Rijnland Hospital, Leiderdorp, The Netherlands

Image has been removed
Vascular Dementia
Vascular Dementia

- Stepwise progression of symptoms secondary to recurrent strokes
- Gradual progression of symptoms due to subclinical ischemia and progressive accumulation of “non specific T2 white matter hyperintensities“
- Often coexists with Alzheimer’s pathology
Frontotemporal Dementia – 3 Major Subtypes

- Prominent behavioral change and disordered social conduct
- Progressive nonfluent aphasia
- Impaired understanding of word meaning and/or object identity
Frontotemporal Dementia

- Memory and visuospatial skills relatively preserved early
- Pathology – Pick bodies and other various neuronal and glial inclusions
- Onset often before age 65.
- Some cases exhibit autosomal dominant inheritance
- Minority have co-existent motor neuron disease
Divorced 60 y.o female – live alone

- 2 years ago fired from her job as dental assistant
- Family concerned because she is frequenting bars late at night – never did this before
- Has become obsessed with getting back with husband
- Beginning to have word finding problems
- Etiology thought to be depression
Diffuse Lewy Body Disease

- Impairment in memory, attention, executive function and visuospatial ability
- Parkinsonism
- Visual hallucinations
- Fluctuating cognition with pronounced variations in attention and alertness
- Pathology - Lewy bodies (intraneuronal cytoplasmic inclusions containing alpha-synuclein)
69 y.o. Innkeeper

- 9 months ago family noticed he seemed confused while on a cruise.
- Confusion has worsened since
- Has started to see imaginary people on property next door
- No longer can plan meals
- Up at night wandering
- Gait has noticeably slowed and he is starting to shuffle
Normal Pressure Hydrocephalus

- Ataxia
- Urinary incontinence
- Dementia
NPH
Rapidly Progressive Dementia (weeks to months)

- Creutzfeldt - Jakob disease
- Toxic/metabolic
- Infectious
- Autoimmune
- Paraneoplastic
- Neurodegenerative
Dementia Evaluation

- Hx from pt and informant - review drug list
- PE including cognitive testing
- Screen for depression
- CBC, CMP, TSH, B12
- Brain image - CT or MRI
- Consider LP if rapidly progressive
- Consider neuropsych testing
- Consider EEG if ? seizures or CJD
- Consider PET scan
History

- Start with the onset of the first cognitive symptom then develop a detailed description for the evolution of all subsequent areas of cognitive decline

- Query all domains

- History from patient and informant
Core Elements of Declining Cognition (Domains)

- Memory – misplaces things, repeats, forgets conversations and appointments
- Speech – expressive speech +/- or comprehension
- Behavior and personality (apathetic, disinhibited, argumentative, compulsive, paranoid)
- Visuospatial – gets lost, difficulty dressing, hallucinations
- Executive – inability to make decisions, solve problems, complete complex tasks, handle gadgets
Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting

Alzheimer’s & Dementia - (2013) 1–10
What Is the Best Dementia Screening Instrument for General Practitioners to Use?


- GPCOG- General Practitioner Assessment of Cognition
- Mini-Cog
- MIS

Other Cognitive Tests

- **Mini Mental State** - copyright restricted, relatively insensitive to mild cognitive impairment and non AD dementias

- **Montreal Cognitive Assessment** - more sensitive for frontal-executive function

- **St Louis University Mental Status Examination** (SLUMS)
Neuropsychological Testing

- Labor intensive and relatively expensive but useful in certain settings (ex. early or young onset)
MRI and/or CT Brain

- R/O treatable pathology
- Pattern of atrophy ? Frontal, hippocampal, parietal
Subfrontal Meningioma
Parietal Atrophy
Central and Cortical Atrophy
Hippocampal Atrophy
Frontotemporal Dementia
Conclusions: Treatment of dementia with cholinesterase inhibitors and memantine can result in statistically significant but clinically marginal improvement in measures of cognition and global assessment of dementia.

Cholinesterase Inhibitors and Memantine

- Does the medication improve my patient’s quality of life?
- Is the improvement worth the cost?
- What about side effects? (G.I., nightmares?)
Syncope and Its Consequences in Patients With Dementia Receiving Cholinesterase Inhibitors

A Population-Based Cohort Study
Sudeep S. Gill, MD, MSc; Geoffrey M. Anderson, MD, PhD; Hadas D. Fischer, MD; Chaim M. Bell, MD, PhD; Ping Li, PhD; Sharon-Lise T. Normand, PhD; Paula A. Rochon, MD, MPH

ARCH INTERN MED/VOL 169 (NO. 9), MAY 11, 2009
Dementia
Performance
Measurement Set

PCPI Approved October 2011
Dementia Performance Measurement Set

- Staging of dementia
- Cognitive assessment
- Functional status assessment
- Neuropsychiatric symptom assessment
- Management of neuropsychiatric symptoms
- Screening for depressive symptoms
- Counseling regarding safety concerns
- Counseling regarding risks of driving
- Palliative care counseling and advance care planning
- Caregiver education and support
Pharmacological Treatment of Neuropsychiatric Symptoms of Dementia
A Review of the Evidence

Kaycee M. Sink, MD
Karen F. Holden, MD
Kristine Yaffe, MD

JAMA, February 2, 2005—Vol 293, No. 5
Alz.org

- Cognitive and informant assessment tools
- Diagnostic guidelines and suggested w/u
- 7 stages of Alzheimers
- Differential dx with links to other degenerative disease sites
- Section on managing challenging behaviors
- Links to clinical studies
Dominantly Inherited Alzheimer’s Network (DIAN)

- Worldwide network of autosomal dominant Alzheimer’s disease centers
Clinical and Biomarker Changes in Dominantly Inherited Alzheimer's Disease

Randall J. Bateman, M.D., Chengjie Xiong, Ph.D., Tammie L.S. Benzinger, M.D., Ph.D., Anne M. Fagan, Ph.D., Alison Goate, Ph.D., Nick C. Fox, M.D., Daniel S. Marcus, Ph.D., Nigel J. Cairns, Ph.D., Xianyun Xie, M.S., Tyler M. Blazey, B.S., David M. Holtzman, M.D., Anna Santacruz, B.S., Virginia Buckles, Ph.D., Angela Oliver, R.N., Krista Moulder, Ph.D., Paul S. Aisen, M.D., Bernardino Ghetti, M.D., William E. Klunk, M.D., Eric McDade, M.D., Ralph N. Martins, Ph.D., Colin L. Masters, M.D., Richard Mayeux, M.D., John M. Ringman, M.D., Martin N. Rossor, M.D., Peter R. Schofield, Ph.D., D.Sc., Reisa A. Sperling, M.D., Stephen Salloway, M.D., John C. Morris, M.D., for the Dominantly Inherited Alzheimer Network

N Engl J Med
Volume 367(9):795-804
August 30, 2012
Clinical and Biomarker Changes in Dominantly Inherited Alzheimer’s Disease

- Concentration of amyloid in CSF begins to decline 25 years before expected onset of sx.
- Amyloid beta detected by PET (PiB) 15 years before.
- Increase in CSF tau and atrophy on MRI 15 years before.
- Cerebral hypometabolism (FDG PET) and impaired episodic memory 10 years before.
- Global cognitive impairment 5 years before.
Alzheimer 1864-1915

Image has been removed
Resources

- Caregiver & Family Resources
  - Alzheimer’s Association
    - Multiple sources of assistance
    - 24/7 Helpline 1-800-272-3900
  - Knowing the signs of caregiver stress
  - Respite Care
    - Private Duty Agencies
    - Assisted Living for overnight stays
    - Adult Day Care
Resources

- Patient
  - Driving Evaluations to assess competency
    - Good Shepherd
      - Ph: 610-776-3517, Fax: 610-776-8375
  - Power of Attorney & Living Will
  - In-home help
    - Referral to County Aging office if over 60
      - Lehigh County: 610-782-3034
      - Northampton County: 610-559-3270
Down’s Syndrome and AD

- 1929 - senile plaques noted in brains of relatively young subjects.

- 1948 - some patients with Down’s syndrome noted to develop Alzheimer type dementia in their 30’s and 40’s.


- Mid 1980’s - Woman in Nottingham England alerts Alzheimer’s researcher at St. Mary’s Hospital in London to high incidence of AD in her father’s family. Mutated gene found to reside on chromosome 21.