Dementia:
Diagnostic Evaluation
and
Medical Treatment of Cognitive Dysfunction

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May 17, 2013

Learning Objectives 1
• Apply standard diagnostic criteria for mild cognitive impairment, dementia, and Alzheimer’s disease
• Review the most common causes of dementia anticipated in primary care or geriatric care settings.
• Discuss the role for dementia screening, quantification of cognitive loss, and formal neuropsychological assessment.

Learning Objectives 2
• Implement standard guidelines for the laboratory investigation of patients with dementia or suspected dementia.
• Review the standard pharmacotherapy for cognitive deficits experienced by patients with mild cognitive impairment and dementia.

Potential Objectives on which this presentation will NOT focus
• Describe the Staging and Natural History of Dementia.
• Describe developing treatment technologies under study for Alzheimer’s disease.
• Incorporate General Treatment Principles of Care into the treatment plans for Patients with dementia.
• Discuss nonpharmacologic approaches to treatment of patients with dementia.
• Integrate nonpharmacologic and pharmacologic treatment options into the treatment of the Behavioral and Psychological Symptoms of Dementia
• Provide optimal education and support for caregivers of those with dementia.

The Dementia Syndrome
• The dementia syndrome is a chronic acquired decline in memory and in at least one other cognitive function (eg, language, visual-spatial, executive) sufficient to affect daily life.
• Cognitive Dysfunction and Amnesia must be demonstrated before a diagnosis of dementia can be given.
• Functional impact must be demonstrated.

DSM-IV Diagnostic Criteria of Dementia
A. The development of multiple cognitive deficits manifested by both:
   1. Memory impairment (learning new information or recall previously learned information)
   2. One or more of the following cognitive disturbances:
      a) aphasia
      b) apraxia
      c) agnosia
      d) disturbance in executive functioning
B. The cognitive deficits cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.
C. The deficits do not occur exclusively in the setting of delirium.
NIA-NINCDS Criteria for MCI

- Concern about a change in cognition, in comparison with the person’s previous level.
- Lower performance in one or more cognitive domains that is greater than would be expected for the patient’s age and educational background
- Preservation of independence in functional abilities
- No evidence of a significant impairment in social or occupational functioning (not demented)

New Terminology DSM V

<table>
<thead>
<tr>
<th>New Term</th>
<th>Similar Old Term</th>
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</thead>
<tbody>
<tr>
<td>Major Neurocognitive Disorder</td>
<td>Dementia</td>
</tr>
<tr>
<td>Minor Neurocognitive Disorder</td>
<td>Mild Cognitive Impairment (MCI)</td>
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<tr>
<td></td>
<td>Cognitive Impairment, No Dementia</td>
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<td>Age-related cognitive decline (ARCD)</td>
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Screening For Dementia

- The US Preventive Services Task Force concluded in 2003 that the evidence is insufficient to recommend for or against routine screening for dementia in older adults.
- CMS has established detection of cognitive impairments as a required element of the first Annual Wellness Visit (G0438) and subsequent Annual Wellness Visits (G0439).
- “…an assessment of an individual’s cognitive function by direct observation.”

Bedside Tools Useful for Screening

- GPCOG
- Mini-Cog
- Memory Impairment Screen (MIS)

Proposed Scheme for the Medicare Annual Wellness Visit

Illnesses Causing Dementia

The Not-Nearly Exhaustive Full List

<table>
<thead>
<tr>
<th>Disease</th>
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<th>Disease</th>
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</thead>
<tbody>
<tr>
<td>Alzheimer’s disease</td>
<td>Creutzfeldt-Jakob disease</td>
<td>Brain Tumor</td>
</tr>
<tr>
<td>Vascular dementia</td>
<td>Subdural hematoma</td>
<td>Anoxia</td>
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<tr>
<td>Frontotemporal dementia</td>
<td>Hypoglycemia</td>
<td>Hypoxemia</td>
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<tr>
<td>Lewy Body dementia</td>
<td>Hypothyroidism</td>
<td>Thiamine deficiency</td>
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<tr>
<td>HIV-Associated dementia</td>
<td>Progressive Multifocal Leukoencephalopathy</td>
<td>Gerstmann-Straussler-Scheinker</td>
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<tr>
<td>Huntington’s disease</td>
<td>Niacin deficiency</td>
<td>Fatal familial insomnia</td>
</tr>
<tr>
<td>Dementia pugilistica</td>
<td>Encephalitis</td>
<td>Meningitis</td>
</tr>
<tr>
<td>Corticobasal degeneration</td>
<td>Familial British dementia</td>
<td>Familial Danish dementia</td>
</tr>
</tbody>
</table>
Common Causes of Dementia

*Common Causes of Dementia in USA: Among Those over Age 20*

- Alzheimer’s disease
- Vascular dementia
- Other
- Other

Pathology-based Diagnoses in Florida Brain Bank

- Alzheimer’s disease
- Lewy Body Disease
- Vascular Dementia
- Hippocampal Sclerosis

Neuropediatrics 2007;29:125
Alzheimer Dis Assoc. Disord. 2002;16(5):203

DSM-IV Criteria for Alzheimer’s Disease

- Criteria for Dementia are present.
- The course is characterized by gradual onset and continuing cognitive decline.
- The cognitive deficits are not due to any of the following:
  - other central nervous system disorders that cause dementia
  - systemic conditions that cause dementia
  - substance-induced conditions
- The deficits are not due to delirium.
- The disturbance is not better accounted for by another psychiatric disorder.

Sorting the Differential Behavior Presentations

- Lewy Body Dementia
  - Often diagnosed with Parkinson’s disease
  - Dementia onset within one year of motor symptoms
  - Visual Hallucinations
  - Fluctuating sensorium
- Frontotemporal Dementia
  - Often present with fairly severe behavior problems
  - Early and progressive change in personality with problems modulating behavior and socially inappropriate responses or activities
  - Early and progressive change in language with difficulty with expression of language or naming

Potentially Reversible syndromes

- Depression
- Medications
- Metabolic
  - Vitamin B12 deficiency
  - Thyroid disorders
  - Thiamine deficiency
  - Chronic diseases
- Gastrointestinal disorders
  - Whipples disease
  - Vitamin E deficiency
  - Pellagra
- Structural brain lesions
  - Tumor
  - Subdural hematoma
  - Normal pressure hydrocephalus
- Infections
  - Neurosyphilis
  - HIV/AIDS

Sorting the Differential Using the Laboratory

- Lab Testing for which there seems consensus for assessment of newly recognized dementia
  - CBC, electrolytes, serum calcium, kidney function, liver function
  - Vitamin B12 and folate
  - Thyroid function test
- Selective Lab Testing for persons at risk
  - Glucose
  - HIV
  - Screening for neurosyphilis

Sorting the Differential Using Neuroimaging

- Most guidelines recommend neuroimaging with either CT or MRI when a patient with suspected dementia is first evaluated.
- Neuroimaging may detect 5% of patients for whom bedside assessment would miss a clinically significant structural lesion
- Risk Factors for detection of structural lesion
  - Onset < age 60
  - Focal signs or symptoms
  - Abrupt onset or rapid decline (weeks to months)
  - Predisposing conditions (metastatic cancer, anticoagulation, head trauma)
Sorting the Differential PET Scanning

- FDG PET approved by Medicare for atypical presentation of course of AD in which frontotemporal dementia diagnosis is suspected
- B Amyloid Imaging. Medicare currently does not cover beta-amyloid PET imaging and the MEDCAC panel’s lack of confidence could further deter federal reimbursement.

Other Tests of Interest

- EEG rarely useful sorting out behaviors vs seizures
- CSF tau and amyloid β 42 not currently used in standard evaluation of dementia.
- For patients in whom there is a very high index of suspicion for CJD, the American Academy of Neurology recommends measurement of a CSF 14-3-3 protein.

Quantifying Cognitive Change

- No One Tool is recognized to be best.
- Bedside Quantification of Cognition Tools
  - MMSE (pack of 50 from PAR is $68.00)
  - MoCA (Montreal Cognitive Assessment)
  - SLUMS memory assessment
- Advantages
  - More comprehensive assessment of cognitive domains
  - Can be followed over time to predict problems, natural history, and competency
  - Facilitates communication with colleagues, caregivers, and IDT

Neuropsychological Testing

- It is the Gold Standard against which other methods of assessment are compared.
- Especially helpful in the setting of mild, early disease when bedside testing may lack sensitivity.
- Useful to clarify atypical presentations
- Helpful to quantify and establish cognitive deficits and strengths: driving, capacity, independence
- Can be followed over time.

Pharmacologic Treatment of Cognitive Dysfunction

- Most Guidelines recommend that patients with Alzheimer’s disease receive a trial of a cognitive enhancer.
- Cognitive Enhancers
  - Acetylcholinesterase Inhibitors
    - Donepezil (Aricept™)
    - Galantamine (Razadyne™)
    - Rivastigmine (Exelon™)
  - NMDA antagonist – Memantine (Namenda™)

Acetylcholinesterase Inhibitors

- Plan on a trial of at least three months unless side effects interfere.
- Modest symptomatic benefit for cognition, mood, behavioral symptoms and daily function for one year.
- 10%-25% will show modest global improvement; more will have less clear improvement.
- All three are FDA approved for Alzheimer’s disease of mild and moderate severity. Donepezil approved for severe dementia due to Alzheimer’s disease. Rivastigmine approved for mild to moderate dementia in Parkinson’s disease.
Should Acetylcholinesterase Inhibitors be used for MCI?
- Early treatment may maintain function at higher levels for longer periods of time.
- There is little evidence that Cholinesterase inhibitors affect the progression to dementia.
- Not an FDA-approved indication.
- Cochrane Library review concludes weak evidence overwhelmed by increased risk of adverse events. Systematic Review recommends against their use in MCI.

Cholinesterase Inhibitors Side Effects
- Diarrhea – 5%-15%
- Weight Loss – 3%-5%
- Nausea - 3% - 19%
- Loss of Appetite 2% - 8%
- Syncope 2%
- Caution in those with peptic ulcer disease, asthma, seizures.

Memantine
- FDA Approved for moderate-to-severe dementia due to Alzheimer’s disease
- Modest improvements in cognition as monotherapy over placebo
- There is conflicting evidence on the benefits of memantine when added to stable doses of donepezil in moderate-to-severe dementia due to Alzheimer’s disease.

Memantine Side Effects
- Confusion (6%)
- Dizziness (5%-7%)
- Headache (6%)
- Use cautiously in those with severe hepatic impairment.
- Reduce dose in those with CrCL < 30.

Using Pharmacotherapy to treat the cognitive deficits of dementia
- There is evidence that the cognitive-enhancing effects of these medications may be modestly helpful in a variety of dementia-causing illnesses.
- Monitor the response by eliciting caregivers observation and monitoring cognition and function.
- No clear end point for discontinuation, but American Geriatrics Society currently recommends discontinuation when FAST=7 (loss of speech, locomotion, and consciousness)

Dementia Workup and Treatment Conclusions
- Standard diagnostic criteria are available which improve rigor of the diagnosis of neurocognitive disorders.
- Alzheimer’s disease is, by far, the most common dementia-causing illness in primary care and geriatric settings.
- Formal assessments of cognitive function can facilitate diagnosis, medical management, and care of patients with cognitive disorders.
Dementia Workup and Treatment

Conclusions

- Laboratory evaluation of the patient with cognitive disorders should be guided by common comorbidity and reasonably common reversible disorders.
- Neuroimaging remains controversial, but is recommended in most guidelines.
- FDA-Approved treatments are available for cognitive dysfunction associated with Alzheimer’s disease and Parkinson’s disease.
- The effects of cognitive-enhancing medications are modest and there is a meaningful potential side effect burden.