Diagnosis and Management of Dementias

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Learning Objectives

- Define dementia and describe differential diagnosis of dementia
- Discuss the general evaluation of cognitive impairment
- Compare and contrast various etiologies of Non-Alzheimer’s Dementia
  - Diagnosis
  - Treatment

Background

- Prevalence of dementia
  - 5-10% of population over 65
  - 25-50% of population over 85
- Etiologies of dementia are numerous
  - Neurodegenerative disease the most common
    - AD (50-75%), FTD, DLB, Dementia due to PD/HD
    - Vascular disease (15-30%)
  - Trauma, infection, toxins
DSM-IV-TR Diagnostic Criteria for Dementia

- Multiple cognitive deficits, including impairment in memory, and one or more of the following:
  - Aphasia
  - Apraxia
  - Agnosia
  - Executive dysfunction
- Impairment is severe enough to cause disturbance in functioning.
- Deficits do not occur exclusively during delirium.
- Not better accounted for by another Axis I diagnosis.

DSM 5
Major Neurocognitive D/O

- Significant cognitive decline from previous level of function in one or more domains: Complex Attn, Executive Fx, Learning and Memory, Language, Perceptual-Motor, Social Cognition
- Concerns by pt, caregiver or clinician
- Impairment in Fx on NP testing or Cognitive assessment tool
- Not during delirium
- Not better explained by another Psych Dx

Differential Diagnosis of Dementia

- Diseases associated with dementia
  - AD, VaD, FTD, DLB, CJD, etc.
- “Reversible” conditions appearing like dementia
  - Medical illnesses (hypothyroidism, NPH, B12 def)
  - Psychiatric illnesses (depression, delirium)
  - Substance-induced causes
    - ETOH/drug intoxication or withdrawal
    - Medications
Evaluation of Cognitive Impairment

- Psychiatric Interview
  - Mood, anxiety, psychosis, substance abuse
  - Subjective cognitive/functional deficits
- Collateral informant
  - Acute, progressive, stepwise, fluctuating?
  - Associated with change in mood/behavior?

Evaluation of Cognitive Impairment

- Past Psychiatric/Medical History
- Medications
- Family History
- Social History
  - Educational/occupational background
  - Recent change in social/living environment
  - Recent loss of spouse

Evaluation of Cognitive Impairment

- Mental Status Examination
- Mini-Mental Status Exam (MMSE)
  - Orientation
  - Immediate/recent memory
  - Attention/concentration
  - Comprehension/Language
  - Naming
  - Reading/Writing
  - Construction/visuospatial abilities
Evaluation of Cognitive Impairment

- Other cognitive exam tools/techniques:
  - Clock Drawing
  - MOCA
  - SLUMS
  - Verbal fluency
  - Abstraction: similarities/difference, proverb interpretation
  - Calculations

Work-up of Cognitive Impairment

- Laboratory tests
  - CBC
  - BUN/Cr, Electrolytes, Mg, Phos, Ca
  - Liver profile
  - UA/Urine tox screen
  - TSH
  - B12, Folate
  - RPR/VDRL

Work-up of Cognitive Impairment

- Neuroimaging (CT/MRI): appropriate for routine use in initial evaluation of dementia (Knopman 2001). Especially useful with:
  - H/O trauma
  - Acute onset/atypical presentation
  - Focal neurologic findings, abnormal gait
  - R/O NPH, neoplasm, subdural hematoma
  - Evaluate for cerebrovascular disease, CVA
Work-up of Cognitive Impairment

- **PET**
  - Not recommended for routine use in initial evaluation of dementia (Knopman 2001).
  - Can improve diagnostic accuracy and help differentiate types of dementia.
  - Can help guide treatment planning (Ercoli and Small 2009).
  - Beta Amyloid ligands

- **EEG**
  - Limited utility
  - Delirium: generalized slow wave activity
  - CJD: triphasic, periodic burst pattern
  - Hepatic encephalopathy: triphasic waves

- **Neuropsychological testing**
  - Differentiating normal aging from early dementia/MCI
  - Differentiating types of dementia (AD v. FTD v. VaD)
  - Differentiating dementia from cognitive changes associated with depression
  - Legal concerns
Differentiating Etiologies of Dementia

- Things to consider….
  - Presenting symptoms
  - Longitudinal course
  - Risk factors
  - Exam findings

Cortical v. Subcortical

<table>
<thead>
<tr>
<th></th>
<th>CORTICAL</th>
<th>SUBCORTICAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Alert, healthy</td>
<td>Disheveled, ill</td>
</tr>
<tr>
<td>Activity/Posture</td>
<td>Normal/erect</td>
<td>Slow/Distorted</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>Constructional deficit</td>
<td>Sloppy due to movement problems</td>
</tr>
<tr>
<td>Speech</td>
<td>Normal articulation</td>
<td>Abnormal, dysarthric</td>
</tr>
<tr>
<td>Language</td>
<td>Dyssnomia, paraphrasis</td>
<td>Normal production</td>
</tr>
<tr>
<td>Memory</td>
<td>Disorder of learning</td>
<td>Disorder of retrieval</td>
</tr>
<tr>
<td>Emotional</td>
<td>Apathetic, lacking drive</td>
<td>Unaware, unconcerned</td>
</tr>
</tbody>
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Alzheimer’s Disease: DSM-IV-TR Criteria

- Must meet DSM-IV-TR criteria for dementia plus:
  - Course characterized by *gradual onset and continuing cognitive decline*
  - Cognitive deficits not due to other CNS conditions, systemic conditions, or substances
  - Deficits do not occur exclusively during a delirium
  - Deficits not better accounted for by another Axis I disorder
Alzheimer's Disease

- **Presenting symptoms**
  - Subtle difficulties in recent memory
  - Apathy, loss of interest in activities

- **Longitudinal course**
  - Progressive, continued cognitive decline
  - Behavioral symptoms and psychosis increase with severity of disease

Vascular Dementia: DSM-IV-TR Criteria

- Must meet DSM-IV-TR criteria for dementia plus:
  - Focal neurologic signs/symptoms OR
  - Laboratory evidence (CT/MRI) of cerebrovascular disease judged to be related to the deficits
  - Deficits do not occur exclusively during a delirium nor are they better accounted for by another Axis I

Vascular Dementia

- Second most common etiology of dementia (15-30%)
- **Presenting Symptoms**
  - Variable
  - Memory impairment not always prominent!
  - Executive dysfunction, psychomotor slowing
  - Functional impairment out of proportion to cognitive impairment as seen on MMSE
  - Changes in personality/mood
Vascular Dementia

- **Risk Factors**
  - DM, HTN, HL, CAD, CVA

- **Longitudinal course**
  - Variable
  - Abrupt onset
  - Stepwise deterioration
  - May be gradual, like AD

Vascular Dementia

- **Physical Exam Findings**
  - Hemiparesis/hemisensory deficits
  - Hyperreflexia, extensor plantar response
  - Incontinence
  - Pseudobulbar palsy
  - Pseudobulbar affect
  - Gait abnormalities
  - Visual deficits

Vascular Dementia

- **Mental Status Exam Findings**
  - Emotional lability, depression
  - Memory may be relatively preserved (DSM diagnostic criteria)
  - “Normal” MMSE score
  - Deficits may be seen in clock drawing
  - Poor insight and judgment; abstraction difficulties
Vascular Dementia

- Imaging
  - Cerebrovascular disease on MRI
  - “Patchy” hypometabolic pattern on PET
- Neuropsychological Features
  - Impaired executive function
  - Impaired attention/concentration
  - Impaired psychomotor speed

- Treatment
  - Supportive care, behavioral management
  - Prevention of future strokes
    - Tight control of vascular risk factors
    - Antiplatelet agents
  - Cholinesterase inhibitors and memantine may be beneficial

Frontotemporal Dementia

- Accounts for ~5% dementias
- Focal atrophy of the *frontal/anterior temporal lobes*
- Abnormal function of cytoskeletal protein *tau*
- *Earlier* age of onset (35-75)
- Equally distributed between M/F
Frontotemporal Dementia

- **Presenting Symptoms**
  - Early and progressive change in **personality**
  - Early and progressive change in **language**.

- **Longitudinal Course**
  - Significant impairment in functioning
  - Gradual onset and continuing decline

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Frontotemporal Dementia

- **Exam Findings**
  - Executive dysfunction
  - Poor attention
  - Receptive/expressive dysphasia
  - Behaviorally disinhibited, impulsive, socially inappropriate
  - Apathetic, amotivated

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Frontotemporal Dementia

- **Imaging**
  - PET: frontotemporal hypometabolism with preserved posterior functioning

- **Neuropsychological Features**
  - *FTD v. AD* (Rascovsky et al 2002)
    - Orientation: FTD>AD
    - Verbal/visual memory: FTD>AD
    - Letter fluency: AD>FTD
    - Category fluency: AD>FTD
Frontotemporal Dementia

- Treatment
  - Psychoeducation, supportive care, behavioral management
  - Cholinesterase inhibitors and memantine may not be as beneficial
  - Serotonergic agents can be beneficial for behavioral symptoms, depression

Dementia With Lewy Bodies

- Lewy Bodies
  - Cytoplasmic inclusions; defining lesion in the substantia nigra of pt's with PD
  - May also be found in the cortex (DLB)
  - Second most common type of degenerative dementia (10-15% cases at autopsy)
  - Important to recognize, given pharmacologic mgmt issues

Dementia with Lewy Bodies

- Presenting symptoms
  - Attention, visuospatial abilities, deficits in memory (often later in disease)
  - Fluctuating cognition/alertness—looks like delirium!
  - Spontaneous parkinsonism
  - Recurrent visual hallucinations, well-formed, detailed
  - Neuroleptic sensitivity
  - Falls, syncope
Dementia with Lewy Bodies

- **Longitudinal Course**
  - Progressive decline
  - "1 year rule"
    - Onset of dementia within 1 year of onset of parkinsonism = DLB
    - Onset of dementia >1 year after onset of parkinsonism = Parkinson’s dementia
  - Up to 25% pts with DLB have no EPS at all

- **Exam Findings**
  - Poor attention
  - Delirium-like fluctuations
  - Parkinisorism
    - More postural instability, gait difficulties
    - Less tremor

- **Imaging**
  - PET: pattern similar to AD + occipital hypometabolism

- **Neuropsychological Features**
  - Deficits in attention, visuospatial tasks
  - Memory impaired, partic. later in disease course
  - DLB v. AD (Kraybill et al 2005)
    - Verbal memory: DLB>AD
    - Executive function: AD>DLB
    - Attention: AD>DLB
Dementia with Lewy Bodies

- Treatment
  - Cholinesterase inhibitors for cognitive and psychiatric symptoms
  - Memantine—??
  - Neuroleptic sensitivity
    - Avoid typical antipsychotics
    - If antipsychotics must be used, choose agents with least likelihood of worsening EPS (quetiapine)
    - Start low, go slow

Alcohol-Induced Dementia

- Alcohol has direct and indirect effects on the brain and cognition
  - Korsakoff’s amnestic disorder
  - Alcohol-induced persisting dementia
- Symptoms may improve with abstinence
- Case reports suggest benefit from AchEI
- Open label study suggests benefit from memantine

Dementia due to Parkinson’s Disease

- Dementia occurs in 20-60% of pts with PD
- Executive dysfunction, psychomotor slowing, impaired visuospatial skills, impaired memory (<AD)
- Occurs later in the disease
- Rivastigmine FDA-approved
- Memantine studied
**HIV Associated Dementia**
- Subcortical dementia
- Mental slowing, poor attention/concentration
- Memory impairment
- Apathy/social withdrawal
- Motor deficits
- Tx: HAART, stimulants, behavioral strategies

**Cognitive Impairment due to Schizophrenia**
- Global cognitive performance declines (3 MMSE pts/decade)
- Impaired memory, visuospatial, new learning
- Less impaired naming
- Spared recognition, fluency, clock
- Case reports AchEI/memantine
- Cognitive training

**Conclusion**
- When determining likely etiology of dementia, consider:
  - Presenting symptoms
  - Longitudinal course
  - Exam findings
  - Risk factors
Conclusion

- Distinguishing etiology of dementia can help guide treatment
  - Not all dementias necessarily respond to AchEI and memantine
  - Not all psychotic symptoms require antipsychotic medications
  - Pts with certain dementias may be more sensitive to antipsychotic medication

Conclusion

- ALL patients with dementia, regardless of etiology, will have caregivers in need of psychoeducation, support, and guidance with long term care planning.
- ALZ.org

References

References