Dementia

MHD Clinical Correlation – Neuroscience Block

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Healthy brain aging

- Occasional naming or word finding problems
- Benign retrieval impairments
- Takes longer, but not impaired learning
- Reaction time decreased
- Psychomotor functioning is impaired
- Preservation of global functioning and ADLs
Demographics of dementia

• Alzheimer disease + vascular dementia - 90%

• Demographics of AD
  - AD most common cause of dementia
  - > 65 yrs. of age
  - 6th leading cause of death?
  - 5% at age 65 yrs.; ⅓ by 85 yrs.
  - Currently ~ 5.4 million; by 2050 it will be 14-16 million
  - Reduces life expectancy by one-half

Mild Cognitive Impairment (MCI)

• Demographics
  - Prevalence of ~ 10% > 65yrs
  - Risk state for dementia

• Diagnostic Categories
  - Amnestic MCI
  - Non-amnestic MCI (executive, visuospatial, language)

• Diagnosis
  - Mild impairment of activities of daily living: self reported or informant, impaired cognitive tests
  - Relevance of subjective cognitive concerns (“worried well”)
  - Standard neuropsychological tests
    - Montreal Cognitive Assessment (MoCA) - more useful
    - Mini-Mental State Examination (MMSE) - usually normal
  - Systematic screening (and treatment) - not recommended
Criteria for Dementia

• Interferes with work or activities
• Decline in previous level of functioning
• Not explained by delirium or psychiatric disorder
• Cognitive impairment is detected
  – History from patient or informant
  – Objective cognitive assessment
• Cognitive/behavior impairment (at least 2)
  – Impaired acquisition/remembering new information
  – Impaired visuospatial abilities
  – Impaired language functions
  – Change in behavior/personality
  – Impaired reasoning, poor judgment

Alzheimer Disease - Diagnosis

• Clinical Criteria:
  – “Essential” - impairment in learning new information

• Functional evaluations:
  – Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment (MoCA)

• Laboratory Testing:
  – ROUTINE: CBC, Chemistry profile, Thyroid functions, Serum B12 level
  – NOT ROUTINE: Screening for syphilis, APOE genotyping for AD, Lumber puncture

• Radiological and other Investigations:
  – ROUTINE: CT or MRI of the brain
  – NOT ROUTINE: Volumetric MRI or CT, SPECT scan, PET scan, EEG

Patient video – presented in lecture

Patient who demonstrates a cognitive difficulty
Risk Factors for Alzheimer Disease

- **Age**
  - 3% age 65-74
  - 17% age 75-84
  - 32% age 85 or older

- **Family History**
  - First degree relative – higher risk

- **Apolipoprotein E (APOE) e4 Gene**
  - One allele – 3 fold increased risk
  - Two alleles – 8-12 fold increased risk
  - Incidence of e3 is greatest in the U.S.

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**Appropriate use of Amyloid PET**

- Young onset dementia (< 65 yrs. of age)
- AD is possible diagnosis, but uncertain (Increase diagnostic certainty & alter management)
- Persistent or progressive unexplained MCI

**Not Indicated**

- Already fulfill core criteria for AD and are typical age
- Determine dementia severity
- In asymptomatic individuals or in lieu of genotyping
- Non-medical use (insurance, disability, etc)
Patient video – presented in lecture

Patient who demonstrates a cognitive difficulty

**VCI due to small vessel disease**

**Mixed AD and VCI**
Vascular Cognitive Impairment

- **Clinical Criteria**
  - Memory impairment is not required

- **Classification – Subtypes**
  - Multi-infarct dementia (cortical vascular dementia)
  - Small vessel dementia (subcortical vascular dementia)
  - Strategic infarct dementia
  - Ischemic-hypoperfusion dementia, hemorrhagic dementia, hereditary vascular dementia (CADASIL), AD with cardiovascular disease

- **Classification – Functional**
  - No cognitive profile, but executive function deficit worse than memory
  - AD can’t be ruled out but less likely if <65 yrs. of age

- **Treatment**
  - Address stroke risk factors
  - Anticholinesterase or NMDA inhibitors?

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**Dementia with Lewy Bodies (DLB)**

- **Clinical Criteria**
  - "Essential" - impairment in learning new information

- **Core features**
  - Frontotemporal: impulsive and disinhibited
  - REM sleep behavior disorder (core feature?)
  - Severe neuroleptic sensitivity

- **Suggestive features**
  - REM sleep disorder – melatonin or clonazepam
  - Parkinsonism – levodopa/carbidopa

- **Treatment**
  - Cognition – rivastigmine (and memantine?)
  - Behavior – quetiapine
  - REM sleep disorder – melatonin or clonazepam
  - Parkinsonism – levodopa/carbidopa

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**Patient video – presented in lecture**

Patient who demonstrates a cognitive difficulty
Frontotemporal Dementia (FTD)

- FTD - heterogeneous with distinct clinical phenotypes, but multiple neuropathological substrates
  - Behavioral variant (>50% of FTD cases)
    - Socially inappropriate behavior
    - Early apathy/inertia
    - Early loss of sympathy/empathy
    - Compulsive/ritualistic behavior
    - Hyperorality/dietary changes
  - Neuropsychiatric testing – Executive dysfunction > memory or visuospatial
  - Neuroimaging

- Primary progressive aphasias (majority of remainder)
- Progressive supranuclear palsy (PSP), Corticobasal syndrome (CBS), Argyrophilic grain disease (AGD)

Patient video – presented in lecture

Patient who demonstrates a cognitive difficulty

Modifiable risk factors for dementia

[Diagram showing risk factors for dementia]
Treatment Strategies for AD

- Establish an early/accurate diagnosis of AD
- Treating medical comorbidities
  - (Diabetes, HTN, Depression, Smoking, Obesity, physical inactivity, educational inactivity)
- Ensuring that appropriate services are provided
- Addressing long-term well-being of caregivers
- Early institution of targeted drugs
- Treating behavioral & psychological symptoms

AD Cognitive Treatment

- Mild (Impaired mental ability and mood swings)
  - Rivastigmine, Donepezil, Galantamine
    - Switch to another, if ineffective
- Moderate (Behavioral disturbances are frequent)
  - Rivastigmine, Donepezil, Galantamine
    - Switch to another, if ineffective or add Memantine
- Severe (Physical problems are dominant)
  - Memantine (?), Donepezil

Behavioral and psychological symptoms

Need to perform a Neuropsychological “Checklist”

- Behavioral dysfunction (agitation, aggressiveness, irritability, disinhibition, aberrant motor)
- Psychosis (delusions, hallucinations)
- Mood disturbance (depression, anxiety, elation, apathy)
- Night-time behavior
- Appetite and eating disturbance
Treatment of behavioral and psychological symptoms

- Non-pharmacological
- Pharmacological
  - General tenets
    - Identify and target symptoms (one at a time)
    - Quantify adverse behaviors
    - Remove other causes
    - Sequential, rationale and limited monotherapy
  - Depression (when severe)
  - Anxiety
  - Agitation → black box warnings
  - Psychosis → black box warnings

Pharmacological treatment for non-cognitive symptoms

- Depression
  - Citalopram (Celexa™)
  - Sertraline (Zoloft™)
- Anxiety
  - Trazodone (Desyrel™)
- Psychosis
  - Quetiapine (Seroquel™)*
  - Haloperidol (Haldol™)*
- Agitation and Aggression
  - Citalopram (Celexa™)
  - Trazodone (Desyrel™)
  - Quetiapine (Seroquel™)*

* Antipsychotics are not indicated for the treatment of dementia-related psychosis.

In April 2005, FDA notified healthcare professionals that patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death. Since issuing that notification, FDA has reviewed additional information that indicates the risk is also associated with conventional antipsychotics.

FDA ALERT [6/16/2008]: FDA is notifying healthcare professionals that both conventional and atypical antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis.