A BRIEF LOOK AT DEMENTIA

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Dementia
- Defined as a progressive decline in cognitive function that impairs daily activities.
  - Always includes a memory problem
  - Includes other cognitive areas, like executive function (decision making) or language
  - Severe enough to cause problems with occupational or social abilities
  - Represents a decline from a prior higher level of functioning

Early Signs of Dementia
- Recent memory problems: repeats self, forgets what was heard or read, misplaces things
- Poor decision making, judgment or problem solving; decreased organizational skills
- Difficulty learning new tasks or performing routine tasks
- Problems managing money, balancing checkbook, forgetting to pay bills

Early Signs of Dementia
- Difficulties expressing self (word finding) or participating in conversation
- Getting lost in familiar areas, forgetting known routes while driving
- Changes in personality, mood or behavior
- Over time, all of these problems become more severe

Mild Cognitive Impairment (MCI)

Evaluation of Dementia
- History and exam
- Memory testing (Bedside or formal neuropsychometrics)
- Brain imaging (MRI or CAT scan)
- Blood tests (B12, thyroid)
Causes of Dementia

- Alzheimer's disease (AD) - The most common cause of dementia
- 5.1 million Americans have Alzheimer's disease and that number is expected to rise significantly in coming years as the population ages
- At this time there is no cure for Alzheimer's
- There are some treatments for symptoms
- Much research is being done

Risk factors for developing Alzheimer’s

- Age
- Genetics
- Hypertension, hyperlipidemia, diabetes
- Downs syndrome
- Low levels of physical activity
- Few cognitive pastimes

Stages of AD

Pathology: Plaques and Tangles

- Amyloid plaques
  - Made up of Beta amyloid that in AD is deposited for years before dementia develops
  - Thought to be neurotoxic
- Neurofibrillary tangles
  - Made up of the protein Tau which is crucial for normal neuronal function
  - In AD, Tau becomes altered and neurons die
  - It is thought that Beta amyloid drives Tau abnormalities

Amyloid

- In AD, the amyloid precursor protein (APP) is cleaved first by beta-secretase and then by gamma-secretase to leave insoluble beta amyloid that accumulates in plaques
- Trials of secretase inhibitors failed to show benefit in AD
- Recent studies have suggested that there is a natural clearance of beta amyloid during sleep. Sleep disorders like obstructive sleep apnea may reduce this clearance and accelerate AD.
**Amyloid PET**
- Amyloid in the brain can now be imaged with PET and special tracers
- Although FDA-approved, these scans are not yet routinely used or available
- Uncertain benefit as long as definitive treatment is not available
- It has been shown that the scans can show amyloid deposits years before dementia develops

**Tau**
- Tau is important in the function of microtubules in the neuron
- Microtubules make up the cytoskeleton of the neuron
- In AD, Tau becomes hyper-phosphorylated and becomes unable to maintain the microtubules
- As microtubules detach and disintegrate, the neuron starts to fail and eventually dies

**Alzheimer’s disease: The big picture**

**Treatment of AD**
- No medication has been shown to slow the progression of AD
- Cholinesterase Inhibitors (ChIs)
  - Donepezil (Aricept), Rivastigmine (Exelon), Galantamine (Razadyne)
  - Approved in mild, moderate or severe Alzheimer’s
  - Modest and temporary improvement in memory function and quality of life
  - Side effects may include nausea and diarrhea

- Memantine (Namenda)
  - NMDA antagonist
  - Approved in moderate or severe (but not mild) Alzheimer’s
  - Modest improvement in memory and learning
  - Side effects may include sedation
- Namzaric
  - combination of donepezil and memantine
  - Once daily

- Depression
  - Antidepressants are often prescribed
- Agitation
  - Some medicines can be harmful so they are used very carefully (atypical antipsychotics)
  - Behavioral management techniques
    - Removing doorknobs
    - Frequent snacks and trips to the bathroom
Vascular dementia

- Second most common cause of dementia
- Often combined with other cause like AD
- It is common to have a cognitive problem after a stroke (i.e. aphasia)
- Dementia develops when multiple strokes accumulate over time

Vascular dementia

- Usually a result of multiple stroke risk factors
  - Hypertension
  - Diabetes
  - Smoking
  - Cholesterol
- The nature of the cognitive problem is referable to the location of the strokes
- Progression of deficits can be gradual or “stepwise”

Vascular dementia: Treatment

- Treatment the underlying cause of stroke if identified
  - Atrial fibrillation
  - Carotid disease
- Address risk factors
  - Hypertension
  - Cholesterol
  - Smoking
- Antiplatelet therapy like aspirin

Vascular dementia: Treatment

- Rehabilitation
  - Speech therapy
  - Cognitive rehab
  - OT and PT
- Address depression
- Cholinesterase inhibitors and Namenda have demonstrated modest benefit

Frontotemporal dementia (FTD)

- Personality change is the most obvious early feature of FTD
- Memory may be preserved early (unlike AD)
- Broad spectrum of symptoms
  - Disinhibited, overactive and restless
  - Apathetic, lacking motivation and initiative
  - Inappropriate, tactless and socially isolated
  - Self-centered, lacking empathy and insight, impulsive
  - Obsessions, compulsions, overeating
  - Disobey social norms

Frontal lobe function

- The frontal lobes are important for executive function, decision making, judgment and insight
- In FTD, the frontal lobes are degenerating resulting in loss of these cognitive functions
- Tau pathology (but not amyloid)
FTD Treatment

- No FDA approved treatments
- Symptomatic treatment
  - Impulsiveness, apathy and depression may respond to SSRIs (sertraline)
  - Disruptive and aggressive behaviors may respond to atypical antipsychotics (quetiapine)
  - Studies have shown no benefit from cholinesterase inhibitors or Namenda
- Caregiver support (often with respite care) is essential

AD vs. FTD PET

Lewy Body Dementia

- Early symptoms are problems with attention, executive and visuospatial function
- Memory often better than early AD
- Special clinical features:
  - Fluctuating cognition
  - Visual hallucinations
  - Parkinsonism
  - REM sleep behavior disorder
  - Neuroleptic sensitivity

Lewy Body Dementia (LBD)

- Occurs on a spectrum with Parkinson's disease
- When dementia precedes PD -> LBD
- When PD precedes dementia -> PDD, PAD
- Pathologic protein associated with all of these is alpha-synuclein

DAT scan

Lewy Body Dementia: treatment

- No FDA approved treatments for LBD
- LBD patients may have a better response to cholinesterase inhibitors than AD patients
- Benefit of Namenda is uncertain
- Minimize the use of antipsychotics
  - Quetiapine may be the best option
- Use levodopa cautiously for parkinsonism since it may worsen hallucinations
  - Try to avoid other Parkinson's medications like Mirapex, Requip, amantadine, silegeline
- Minimize anticholinergic use for bladder incontinence like Ditropan and Detrol
Common Dementias

<table>
<thead>
<tr>
<th>Dementia Type</th>
<th>Early Symptoms</th>
<th>Lobes</th>
<th>Meds</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>Memory</td>
<td>Temporal, Parietal</td>
<td>Ch, Namenda</td>
<td>Beta-Amyloid, Tau</td>
</tr>
<tr>
<td>VD</td>
<td>Variable</td>
<td>Any</td>
<td>Aspirin</td>
<td>NA</td>
</tr>
<tr>
<td>FTD</td>
<td>Personality, executive</td>
<td>Frontal, Temporal</td>
<td>SSRIs</td>
<td>Tau</td>
</tr>
<tr>
<td>LBD</td>
<td>Attention, parkinsonism, hallucinations</td>
<td>All</td>
<td>Ch</td>
<td>Alpha-synuclein</td>
</tr>
</tbody>
</table>

General treatment of Dementia

- Exercise
  - Walking, yoga, water aerobics, ballroom dancing
- Cognitive leisure activities
  - Board games, cards games
  - Crossword puzzles, Sudoku
  - Reading
  - Playing musical instruments
- Social interaction
  - Day programs
- Social work referral
  - POA
  - Community resources

Caregiver Stress

- Taking care of a loved one with dementia is challenging
  - You may be cut off from friends, leisure activities and other responsibilities
  - It may lead to fatigue, depression and sleep problems
- Educate yourself
  - Learn about dementia and what the future may bring
  - Find out what services your community has to offer
  - Find a support group in your area
- Take care of yourself
  - Eat well. Get enough sleep and exercise.
  - Ask for help from family and friends
  - Consider respite services
  - ADRC, Curative Rehab, Alzheimer's Association

Decision to stop driving

Dementia and driving

- People with dementia are at increased risk for accidents
- Those with dementia overestimate their ability to drive safely
- They may be resistant to the suggestion that they should stop driving
- Most authorities suggest that patients with even mild dementia should stop driving
- Consider a driving evaluation

Signs of unsafe driving

- Difficulty navigating to familiar places
- Poor lane control
- Confusing the brake and gas pedals
- Failing to observe traffic signs
- Making slow or poor decisions
- Hitting the curb
- Inappropriate speed
- Getting angry or confused while driving

Question 1

- A 65-year-old retired teacher claims that she is forgetful. She misplaces her cell phone. She needs to write things down or she will forget. She drives, manages her finances and attends to her ADLs independently. Her MRI and blood tests are normal. Her mental status testing shows mild memory difficulty. What is her diagnosis?
  - A. Alzheimer's disease
  - B. Frontotemporal dementia
  - C. Mild cognitive impairment
  - D. Vascular dementia

Answer 1

- Mild cognitive impairment (MCI)
  - She has memory concerns and her mental status testing confirms slight memory impairment. However, it is not severe enough to affect her independence.
  - She has a 10-15% per year risk of developing dementia, usually Alzheimer's. So her 5 year risk is about 50%.
  - She should have an annual follow-up visit to monitor her status.
Question 2

- An 80-year-old man was diagnosed with AD two years ago. He is no longer driving or managing finances. He lives at home under the supervision of his spouse and his daughter, who lives nearby, checks on him daily. In addition to memory problems, he is having some personality changes, confusion and occasional wandering. He requires some assistance with ADLs. What medications are FDA approved at this point?
  - A. Cholinesterase inhibitors (Aricept, Exelon, Razadyne)
  - B. Memantine (Namenda)
  - C. Ginkgo biloba
  - D. A and B

Answer 2

- Cholinesterase inhibitors and Namenda
  - The patient meets criteria for moderate Alzheimer's disease.
  - CIs are approved for mild, moderate or severe AD.
  - Namenda is approved for moderate or severe AD.
  - CIs are often started early and Namenda is often added later.
  - Evidence does not support the use of ginkgo biloba, although many patients try it. It can be associated with several drug interactions so it is important to ask about supplements.

Question 3

- An 80-year-old woman has a two-year history of gradual cognitive decline. She has started to have periods where she just sits in a chair and stares straight ahead and is difficult to arouse. She claims to see her deceased mother washing dishes. She shuffles when she walks but has had no falls. Rarely, she acts out her dreams. She has occasional urinary incontinence. What is the best medication to prescribe?
  - A. Detrol for urinary incontinence
  - B. Haldol for hallucinations
  - C. Levodopa for Parkinson’s
  - D. Aricept for cognition and attention

Answer 3

- Aricept for cognition and attention
  - The diagnosis is Lewy body dementia (LBD) based on her dementia, parkinsonism, hallucinations, fluctuations in attention and REM sleep disorder.
  - LBD patient’s often have a very good response to cholinesterase inhibitors (Aricept) so this should be tried
  - Anticholinergics like Detrol often worsen cognition
  - Antipsychotics like Haldol may cause a severe paradoxical response
  - Levodopa may help the mild parkinsonism but could worsen hallucinations so I would avoid at this point

Question 4

- A 75-year-old woman has a history of hypertension, diabetes and smoking. One year ago she had a stroke of the left hemisphere leaving her with mild aphasia and right-sided weakness. Since then, she has had a steady decline in her memory and has become withdrawn. What is the least important thing to do for her right now?
  - A. Encourage smoking cessation
  - B. Aggressively treat hypertension and diabetes
  - C. Assess for depression
  - D. Get a PET scan to clarify the diagnosis

Answer 4

- PET scan
  - The patient almost certainly has vascular dementia. An MRI scan would probably demonstrate multiple strokes.
  - Her risk factors should be evaluated and treated appropriately.
  - Depression is common in dementia and following stroke. Treatment of her depression may have a major functional impact.
  - A PET scan here would be of marginal value.
Question 5

- A 65-year-old attorney was recently dismissed from his firm after several episodes of sexually inappropriate behavior. For the past 2 years he has become socially isolated. He watches reruns on TV for hours at a time. He binge eats and has gained 30 pounds. His spouse is desperate in dealing with these changes. He doesn’t seem to care how his behavior has affected his family and his life. MRI of the brain shows frontal atrophy. What is the most appropriate next step?
  - A. Referral to a dietician
  - B. Disable the TV
  - C. Give him a stern lecture about his behavior
  - D. Referral of the patient and caregiver to the Alzheimer’s Association or similar organization for education and caregiver support.

Answer 5

- Referral to the Alzheimer’s Association
  - This diagnosis is frontotemporal dementia
  - Personality and behavioral changes can be dramatic and devastating.
  - Patients usually lack insight and empathy. They often do not respond to logical thinking.
  - Behavioral approaches may be beneficial, but disabling the television may result in hostility.
  - Referral to an appropriate care and support organization can provide much needed education and insight, especially for the caregiver.

Questions?