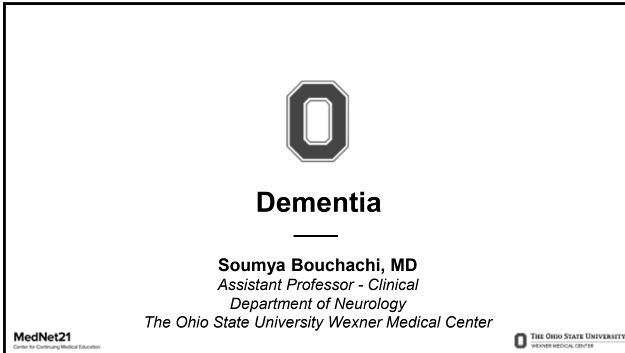

Introduction

- Because of the aging population, the burden of dementia on the economy and society is increasing.
- 5.8 million people age 65 or more in the US are living with AD
- The number is expected to increase to about 14 million by the midcentury

What is dementia?

- DSM-5 definition: Dementia or major neurocognitive disorder is characterized by a significant decline in cognition compared with a previously known cognitive baseline.
- The decline should involve at least 1 of the following cognitive domains: learning and memory, language, executive functions, attention, perceptual motor, or social cognition.
- The cognitive deficits must be significant enough to interfere with activities of daily living.

How to assess a patient with cognitive complaint?

- During the in person assessment, the aim of history taking is to recognize cognitive and behavioral changes in the individual.
- We are looking for an impairment in at least 2 of the following domains:

1. Impaired ability to acquire and remember new information
2. Impaired reasoning and handling of complex tasks and poor judgment
3. Impaired visuospatial abilities
4. Impaired language
5. Changes in personality, behavior, or comportment

- The caregiver need to be interrogated separately in order to avoid uncomfortable situations, as the patient is often unaware of his cognitive or behavioral problems.

Medical history:

- Stroke risk factors
- Autoimmune disorders
- History of cancer
- HIV infection
- Mental illness
- Medication side effects
- Alcohol and drug use

Family history and genetic factors:

- having a first degree with dementia may increase the risk for dementia.
- Some genes can increase the risk of Alzheimer's disease. APoE4, APP gene and Presenilin 1 and 2 genes.
- Some genes increase the risk for frontotemporal dementia such as C9ORF and MAPT genes.

Neurological exam:

- We look for a parkinsonian syndrome, gait problems, frontal release signs, eye movements abnormalities, abnormal movements, change in vision, focal neurological signs.
- We also look for symptoms of systemic diseases such as skin lesions, joint swelling
- signs of hypoxia, liver dysfunction, abnormal sleepiness during evaluation.

- Simple cognitive assessments such as MMSE, SAGE or MOCA can be very helpful.
- Blood work can be ordered to rule out reversible causes of dementia such as b12 deficiency, hypothyroid, metabolic encephalopathies, systemic diseases and infectious causes such as syphilis.

7. Copy this picture:

- Complete the work up by a brain imaging: A brain MRI which can reveal significant regional volume loss, cerebrovascular disease, brain metastasis, changes in basal ganglia, hydrocephalus.
- Other imaging modalities can be very helpful, such as FDG PET scan of the brain and DAT scan.

What are the most common causes of dementia?

Alzheimer's disease:

- Is the most common cause of dementia.
- Characterized by short term memory problem, visuo-spatial problems and executive dysfunction.
- It is considered early onset when it starts prior to 65 and late onset when it starts after 65.
- The neurological exam: non focal, apraxia
- Brain MRI : hippocampal atrophy, generalized volume loss.
- The FDG PET scan: decrease in the metabolism in the temporal and parietal areas.

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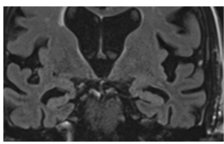
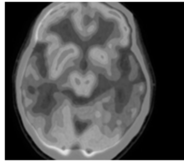




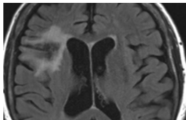
The treatment: symptomatic, includes Cholinesterase inhibitors, NMDA antagonists.

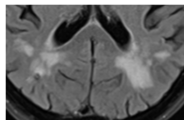
2 disease modifying therapies have been recently approved by the FDA:

- Aducanumab and Lecanemab: target the amyloid plaques. Very modest benefit. They slow down the progression by about 25.
- Other medications: used to treat the behavioral symptoms such as antidepressants, mood stabilizers and antipsychotics.

Vascular dementia:

- Have the same risk factors as strokes.
- Can progress gradually, but typically progresses in a stepwise manner.
- Can be caused by strokes in strategic areas of the brain.





- The symptoms depend on affected brain areas, however, patients most of time have problems with executive functions
- We look for history of strokes or TIAs, uncontrolled HTN or diabetes.
- On the exam: we look for focal signs, such as weakness, visual field cut or language problems
- Treatment: aims to slow down or stabilize the progression by treating the risk factors such as HTN, diabetes, dyslipidemia and arrhythmia.

Dementia with Lewy body:

- Starts progressively after 65.
- Characterized by visual hallucinations, fluctuation of symptoms. The progression is usually more rapid than Alzheimer's.
- Exam: parkinsonian syndrome.
- MRI: the structural changes are usually minimal
- FDG PET scan: decreased metabolism in the posterior parts of the brain
- Treatment is mainly symptomatic: cholinesterase inhibitors.

- Frontotemporal dementia
- bvFTD : changes in personality, impulsiveness, apathy, loss of interest in enjoyable activities, loss of empathy, inappropriate behavior.
- The cognitive problems may be very mild or even absent at the beginning.
- Need for history from the family as the symptoms can easily be missed.
- Primary progressive aphasias are also variants of FTD and manifest with language problems.
- nfFTD: problem with expressing language, significant agrammatism.
- svFTD: problem with understanding language and patients lose the meaning of words.

- MRI: atrophy of the frontal and temporal lobes.
- FDG PET scan: can reveal decrease in the metabolism in the same regions.
- Treatment: symptomatic and includes SSRIs and antipsychotics.

Other degenerative dementias:

- Cortico-basal degeneration: characterized by an asymmetric parkinsonian syndrome, problems with proprioception, alien hand phenomenon .
- PSP: characterized by a parkinsonian syndrome, paralysis of the vertical gaze, gait problems and tendency to fall backward.
- Chronic traumatic encephalopathy: is characterized by history of multiple traumas or concussions. The behavioral changes are very frequent. The progression is similar to Alzheimer's disease.

Infectious causes of dementias:

- Include HIV, syphilis, PML, CJD

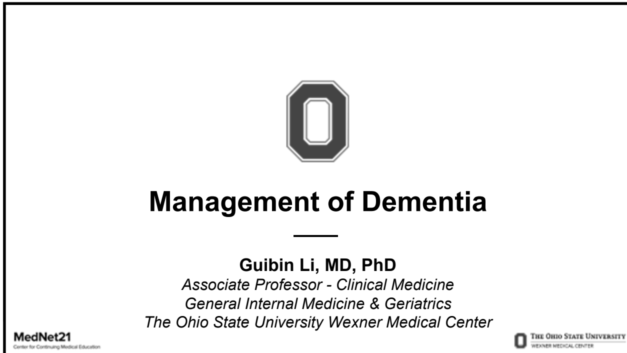
Normal pressure hydrocephalus:

- Is characterized by the triad Cognitive impairment, gait apraxia and urinary incontinence.
- A lumbar puncture can reverse the gait problems but not the cognitive problems.
- The best candidates for the procedure are patient with severe gait problems and mild cognitive issues.

Potentially treatable causes of dementia

- Vitamin deficiencies: B12 and B1. We look for history of weight loss, malnutrition or alcohol abuse.
- Endocrine disorders: hypothyroid, parathyroid problems, adrenal problems
- Metabolic problems: uremia, hepatic dysfunction, cardio-pulmonary failure.
- Autoimmune/inflammatory/paraneoplastic causes : usually acute or rapidly progressive. The symptoms are largely variable and may include cognitive, behavioral changes, seizures, focal neurological signs.

- Psychiatric illnesses: depression can manifest as pseudo-dementia in elderly.
- Medication side effects: treatment of psychiatric illnesses can affect cognitive functions, anticholinergic medications, benzodiazepines and opiates.
- Cancers: brain metastasis, brain tumors, mass effect. Paraneoplastic syndromes.



Objectives

- Be familiar with non-pharmacologic interventions for management of dementia
- Understand how to manage non-cognitive symptoms in patients with dementia

Outline

- Pharmacologic therapy
- Nonpharmacologic interventions
- Nutrition
- Address polypharmacy
- Reduce cardiovascular risk factors
- Manage neuropsychiatric symptoms
- Caregiver support

Pharmacologic Therapy for Alzheimer's Disease

Medications	Year Approved	Mechanism of Action	Indications	Major Side Effects
Donepezil	1996	Cholinesterase inhibitor	Mild to severe AD	GI symptoms Bradycardia
Rivastigmine	2000	Cholinesterase inhibitor	Mild to severe AD Mild to moderate PD dementia	GI symptoms Bradycardia
Galantamine	2001	Cholinesterase inhibitor	Mild to moderate AD	GI symptoms Bradycardia
Memantine	2003	NMDA receptor antagonist	Moderate to severe AD	Dizziness, constipation, headaches
Aducanumab	2021	Anti-amyloid monoclonal antibody	CDR 0.5 to 1	ARIA, headaches and falls

NMDA: *N*-methyl-D-aspartate. ARIA: amyloid-related imaging abnormalities. CDR: Clinical dementia rating

Nonpharmacologic Approaches

Measures	Examples	Potential Benefits
Physical exercises	Walking Strength exercises Tai chi	Slow down the progression of physical decline Reduce falls
Cognitive exercises	Readings, video games, puzzles Learn something new	Maintain memory and cognitive function
Social interactions	Group activities with friends Attend family events Volunteer work	May reduce rates of disability and risk for depression
Diet Modification	A balanced diet	Reduce cardiovascular risk Maintain a healthy weight

Address Polypharmacy

- Avoid medications that may cause cognitive impairment
  - -Medications with anticholinergic effects
  - -Benzodiazepine
  - -Opioids
  - -Antipsychotic drugs
- Reduce pill burden
  - -Discontinue unnecessary or ineffective medications
- Do not prescribe medications to treat side effects of other medications

Reduce Cardiovascular Risk Factors

- Hypertension
- Diabetes
- Orthostatic hypotension
- History of TIA or CVS-antiplatelet therapy
- Hyperlipidemia
  - -Statin therapy
  - History of CVA and TIA-statin therapy
  - No history of CVA and TIA-follow the primary prevention of CVD based on ASCVD risk

Nutrition

- Weight gain is less common in patients with dementia
- Weight loss is common, especially in patients with advanced dementia
  - - Decreased sensation of taste/smell
  - - Loss of ability to prepare meals
  - - Oral/pharyngeal dysphagia
  - - Dental issues
  - - Unable to eat independently

Management of Weight Loss

- Discontinue medications that may cause weight loss
- Enhance the taste and flavor of food
- Speech therapy for swallowing evaluation
- Management of dental problems
- High-calorie supplements-can promote weight gain
- Appetite stimulants-low quality evidence
- Oral assisted feeding is recommended
- Long term tube feeding should not be recommended in patients with advanced dementia

Neuropsychiatric Symptoms

- More challenging than cognitive symptoms
- Significant impact on quality-of-life and caregiver burden
- Common symptoms include depression, behavioral disturbances and sleep disorder
- 80-90 % of patients have one or more of these symptoms
- Behavioral disturbances are leading factors for nursing home placement

Depression

- Common in patients with early stage of dementia
- Selective serotonin reuptake inhibitors
  - -Citalopram, not exceed 20 mg daily
    - Should be avoided if QTc greater than 500
  - -Sertraline
  - -Escitalopram
- Tricyclics should be avoided

Sleep Disorder

- Circadian rhythm disturbance
- Nonpharmacologic approaches
  - -Encourage regular daytime activity to improve nighttime sleep
  - -Minimize daytime napping
  - -Have consistent bedtime routine
  - -Make sure environment is comfortable
  - -Natural light therapy
- Pharmacologic therapy
  - -Melatonin
  - -Trazadone
  - -Mirtazapine

Behavioral Disturbances

- Including delusion, hallucinations, agitation/aggression, wandering and disinhibition
- Common causes including delirium, medication adverse effects or withdrawal, uncontrolled pain, sleep disturbance
- Evaluate and treat the potentially reversible causes
- Nonpharmacologic approaches- first-line choice
  - Redirection and reassurance
  - Try to accommodate behaviors, not control them
  - Maintain structure by keeping the same routines
  - Provide familiar objects and photographs, especially in a new environment

Behavioral Disturbances

- Medication review
- Assessment and management of pain-often challenging
  - Can start a trial of scheduled pain medication-first with Tylenol
- Pharmacologic therapy
  - Cholinesterase inhibitors
    - Mild to moderate AD with behavioral disturbances
    - Lewy body dementia
  - Antidepressant
    - Citalopram
    - Mirtazapine

Behavioral Disturbances

- Pharmacologic therapy-continued
  - Antipsychotics-not the first line choice
    - Only use if the symptoms have the potential to cause harm to patients or others and if nonpharmacologic approaches have failed
    - FDA requires a "black box" warning for antipsychotics
      - Increased risk of all-cause mortality in elderly patients with dementia
    - Explain side effects of medication to the patient and family before starting
    - Medication choice-olanzapine or quetiapine

Behavioral Disturbances

- Pharmacologic therapy
  - Antipsychotics-continued
    - Should be avoided if QTc greater than 500 or patient is on medications that can prolong QTc
    - Evaluate the symptoms frequently and attempt to wean it off
    - Quetiapine is the preferred agent for patients with PD and Lewy body dementia
  - Mood stabilizer- limited evidence
    - Divalproex (Depakote)- possible option
  - Benzodiazepine and anticholinergic medications should be avoided

Caregiver Support

- Provide counseling for family members and caregivers
  -Coping skills, stress and time management
- Identify sources of volunteer help—family, friends, church
- Schedule regular breaks and respite
- Care coordinators-Social workers and nurses
- Consider local support group and online support resources
  -Alzheimer’s association: https://www.alz.org
  -Resources for Enhancing Alzheimer's Caregiver Health (REACH)
  https://www.nia.nih.gov/research/resource/resources-enhancing-alzheimers-caregiver-health-reach
  -Savvy Caregiver: https://www.caregiver.org/savvy-caregiver-program

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