Team Medicine

22# Dementia

Writer: Sama Al Ohali
Reviser1:MosaedAldekhayel

Leader: Sama Al Ohali

■ Slides ■ Doctors notes ■ Additional

431 Teams

Lecture OUTLINE:

***PART 1:**
Introduction to dementia:
-Difference between dementia and other similar problems
-How to approach a patient with dementia
***PART2:**
-Irreversible causes of dementia
***Cases + Questions**

Part 1

What is Dementia?

- Decline in cognition: **which includes** learning and memory, language, executive function, complex attention, perceptual-motor and social cognition, with preservation of consciousness.
- Represent a decline from previous level of function
- Does not occur exclusively in the context of a delirium
- **Interferes with daily function and independence**
- Not explained by another mental disorder (e.g. major depressive disorder, schizophrenia)
- Demented patients do not forget where they studied elementary school, but they forget what they had for dinner last night.
- There is no cure for dementia.You can only treat symptoms.
- MOST COMMON DEMENTIA IS WITH ALZHEIMERS DISEASE.

What happens in normal aging?(With no dementia, no delirium…etc.)

- Mild changes in memory
- Rate of information processing
- Not progressive
- Not affecting daily function.

- **It is important to differentiate dementia from:**

A -Mild cognitive impairment (MCI)
B –Pseudo-dementia = Depression (severe)
C -Delirium

A) Mild Cognitive Impairment (MCI):

- Deficit in cognition in at least one domain
- **No impairment in activities of daily living**
- Patients with MCI are at increased risk of dementia
- Amnestic MCI has a conversion rate to dementia of 10-15%/year

→ The main difference between MCI and dementia is impairment of daily activity level

B) Depression (pseudo-dementia):

- **Subjective complain about memory loss (the patients)**
- Psychomotor slowing
- **Poor effort on testing ("I can't do this")**

→ Main difference between depression and dementia is the subjective complain about memory loss with pseudo-dementia. Demented patients will never come to you complaining of memory impairment. Another difference is: patients with early dementia will try to follow your commands; they will try their best to show that they are good at what they do. Depressed patients will just keep saying I can't do this or that….

Pseudodementia versus Dementia

Pseudodementia	Dementia
Acute onset	Insidious onset
Family aware	Family unaware at first
Answers "I don't know" when asked questions	Confabulates when asked questions
Will talk about deficits when asked	Will minimize their deficits
Treat with antidepressants	Will not improve with antidepressants

Pseudo-dementia is something that happens quickly and because of that everyone around the patient is going to be aware, and the patient is also going to be aware because it is due to a mood disturbance "depression.
When the patient wants help he will emphasize on his disability, seek medical advices without hiding any information. So when given antidepressants, he will be better.

C) Delirium:

- **Reversible disturbance of *consciousness* with reduced ability to focus, sustain, or shift attention**.
- Not better accounted for by dementia.
- **Hours to days and is fluctuating**
- **Caused by a medical condition, substance intoxication, or medication side effect.**

→ Main difference between delirium and dementia: In delirium there is reversible disturbance of consciousness and in dementia the consciousness is intact. Another difference: delirium patients are different when you see them in the morning than when you see them at night. Demented patients behave are relatively the same throughout the day.

	Delirium "acute confusional state"	Dementia
Onset	Acute , sudden Caused by a medical, or environmental condition.	Slowly gradually progressive Loss of brain cells resulting in decline of day-to-day cognition and functioning.
Duration	Hours to days	Months-Years
Consciousness	Fluctuates (sleepy, somnolent, drowsy,)	Preserved
Cognitive Testing	Vary from poor to good depending on time of day.	Gradually worse over months/years
Memory	Recent and immediate memory impaired. Long term lost	Long term preserved in early disease
Sleep/wake cycle	Disturbed or reversed	Normal to fragmented
Hallucination / delusions	Often of a frightening or paranoid nature	Usually absent. Except in advanced causes or DLB
Prognosis	Treatable and reversible	Progression can be slowed but not reversed.
Treatment	Treat underlying cause. Restore sleep/wake cycle Environment	Cholinesterase inhibitors, memeantine Symptomatic treatment

---

Epidemiology of Dementia:

- 5% of individuals >65 years
- 35-50% of persons >85 years

Clinical Features of Dementia: Patients will have difficulty in:

- Retaining new information (remembering events)
- Handling complex tasks (paying receipts)
- Reasoning (coping with unexpected events)
- Spatial ability and orientation (lost in familiar places)
- Language (word finding)
- Behavior

→ Getting lost in familiar places (in his own house, he does not know where is the washroom)
→ Change in behavior (anxious, very emotional, cries easily)
→Difficulty in retaining new information (if he buys a new phone, it is very difficult for him to remember how to use it)
→ Reasoning (If you ask him if there is fire in the house what are you going to do? He will not know what to do)

Risk Factors of Dementia

-Age: **(Most important factor)**
-Affected 1st degree relatives:**Some types of dementia are inherited**
-Smoking/Atrial fibrillation/Hypertension/Diabetes/Obesity **→ therefore, physical activity decreases risk of dementia.**

Dementia syndromes

A. *Reversible* (need to be ruled out)
B. Irreversible

A) Reversible Causes of Dementias

- Drug toxicity
- Vitamin B12/Thiamin deficiency
- Infections
- Alcoholism
- Inflammatory states
- Hormonal dysfunction
- Environmental toxins
- Drug abuse
- Depression
- Subdural hematoma
- Hyper- and hypothyroidism

Mnemonic for Reversible Causes of Dementia (DEMENTIA):
Drugs
Endocrine
Metabolic
Emotional
Nutritional
Tumor/Trauma
Infections
Atherosclerosis

B) Irreversible Dementia Syndromes

- Alzheimer disease (AD)
- Dementia with Lewy bodies
- Pick's disease = Frontotemporal dementia
- Vascular dementia
- Parkinson disease with dementia

Diagnostic Approach to Dementia

A) History taking.
B) Physical examination
B) Labs
C) Imaging

A) History taking and physical examination:

What do you ask about in history?

1. Symptoms of dementia
2. Associated neurologic symptoms
3. Associated psychiatric symptoms
4. Course
5. Other medical conditions

1) Symptoms of dementia

Ask caregivers or informant:

- If patient forgets important appointments and family events.
- Does the patient repeat the same question or sentence over and over again in the same conversation?
- Ask about difficulty recognizing family, friends, and famous people?
- Difficulty with simple daily activities (Ex a teacher no longer knows how to revise a students paper)
- Getting lost in familiar places.
- Grammar errors, word finding difficulties, and language problems.
- Ask about change in behaviour, being very emotional, or personality aggressiveness.

2) Associated neurologic symptoms

- Slurred speech
- Focal weakness
- Walking difficulties
- Imbalance

→ If tremor and gait problems: Think of Parkinson's… If slurred speech and focal weakness: think of vascular dementia…. If imbalance and walking difficulties: think of vitB12 related dementia.

3) Associated psychiatric symptoms

- Depression: hopelessness, worse in morning, suicidal thoughts
- Psychotic features: delusions and hallucinations
- Ask about low mood and crying.
- Losing/Gaining weight

What is the difference between Illusion, Hallucination, and Delusion?

-Illusion= Misperception. There is a stimulus but you perceive it in a wrong way
-Hallucination= Perception without external stimulus

Ex: you enter a dark room and you feel there is a ghost but when you put the light on you find nothing → hallucination…
If you open the light you see your friend→ it is an illusion.

-Delusion: firm false beliefs, which are held very strongly, in spite of evidence to contrary.

Ex: Someone thinks "the Russians are trying to poison him with radioactive particles delivered through his tap water"

4) Course: stability or deterioration depends on etiology

- **Very important determinant of the cause**
- Rapid progressive vs. slow gradual decline
- Gradual onset of short term memory loss (Alzheimer Disease)
- Sudden, step wise deterioration (vascular)

5) Associated medical conditions:

- Ask about the causes of reversible dementia

- Vascular risk factors: HTN, DM, stroke
- Thyroid disorders
- Anemia
- Depression

B) Physical Examination:

- Look for Focal neurological deficit
- Signs of Parkinson disease (PD) (e.g. cogwheel rigidity and/or tremors)
- Gait (Parkinson, vascular, NPH…)
- Also assess the cognitive function of the patient → there are multiple screening tests, the most commonly used is the MMSE.

Cognitive Function Assessment:

1-Mini-Mental State Exam (MMSE):

- The most widely used
- Tests orientation, registration, recall, attention, calculation, language
- Maximum score is 30 points.
- ***Score of < 24 points is suggestive of dementia or delirium.***
- Sensitivity of 87%, specificity of 82%
- Confounding factors: Age and education, as well as language, motor, and visual impairments

2-Montreal cognitive assessment

3-Informant interview

MMSE: (=Folstein test): is a brief 30-point questionnaire test that is used to screen for cognitive impairment. It is commonly used in medicine to screen for dementia. It is also used to estimate the severity of cognitive impairment and follow the course of cognitive changes in an individual over time, thus making it an effective way to document an individual's response to treatment. It assesses orientation attention, recall, language, and the ability to follow simple verbal and written commands. It is one of the investigations undertaken to assist with establishing a diagnosis of dementia. The MMSE is NOT a tool for diagnosing dementia in its own right.

How to perform the test? http://www.youtube.com/watch?v=J_PxO4f017E

C) Labs: The aim is to rule out any treatable causes:

- CBC, differential (anemia, chronic infection)
- Thyroid function test
- Vitamin B12, thiamine
- VDRL (Neurosyphilis)
- CSF

D) Neuroimaging: Brain CT or MRI is the routine initial evaluation for every patient with dementia, to rule out reversible causes:

- Subdural hematoma
- Normal pressure hydrocephalus

Part 2

#Alzheimer Disease (AD):

- A neurodegenerative disorder of **uncertain cause** and pathogenesis that **primarily affects older adults.**
- **Most common cause of dementia**.
- **Slightly more common in women.**
- **Incurable** conditions that result in **progressive loss** of function & structure and / or death of neurons
- A disease of older age, rarely occurring <60
- 5% are inherited, present before 65
- **Main clinical manifestations of AD are selective memory impairment and dementia**

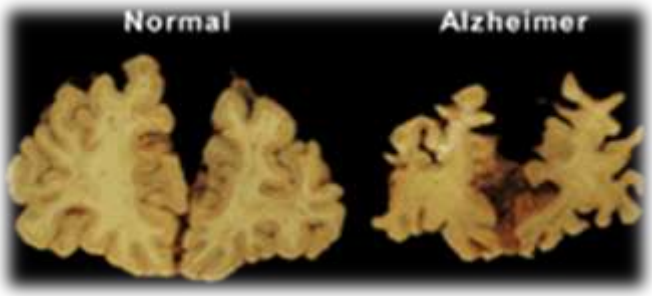
DSM-5 criteria for major neurocognitive disorder due to Alzheimer disease

A. Evidence of significant cognitive decline from a previous level of performance in one or more cognitive domains*:
Learning and memory.
Language.
Executive function.
Complex attention.
Perceptual-motor.
Social cognition.
B. The cognitive deficits interfere with independence in everyday activities. At a minimum, assistance should be required with complex instrumental activities of daily living, such as paying bills or managing medications.
C. The cognitive deficits do not occur exclusively in the context of a delirium.
D. The cognitive deficits are not better explained by another mental disorder (eg, major depressive disorder, schizophrenia).
E. There is insidious onset and gradual progression of impairment in at least two cognitive domains.
F. Either of the following:
Evidence of a causative Alzheimer disease genetic mutation from family history or genetic testing.
All three of the following are present:
1) Clear evidence of decline in memory and learning and at least one other cognitive domain.
2) Steadily progressive, gradual decline in cognition, without extended plateaus.
3) No evidence of mixed etiology (ie, absence of other neurodegenerative disorders or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline).

DSM: diagnostic and statistical manual.
* Evidence of decline is based on: Concern of the individual, a knowledgeable informant, or the clinician that there has been a significant decline in cognitive function; and a substantial impairment in cognitive performance, preferably documented by standardized neuropsychological testing or, in its absence, another quantified clinical assessment.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), American Psychiatric Association, Arlington, VA 2013.

UpToDate



Cortical Atrophy
Flattened Sulci
Enlarged Ventricle

Genetics of AD

Early-onset AD

- Accounts for <1% of cases
- Follows an autosomal dominant inheritance pattern
- Mutations in three genes: amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2)

Late-onset AD

- More complex
- the most firmly established genetic risk factor is apoprotein E ε4 (APOE ε4)

Genetic testing is available for the known genes in early-onset AD but has not been widely adopted, because of the lack of highly effective preventative or therapeutic strategies

→**Genetic testing is available. However, usually it is not used because there is no cure.**

Clinical Course of AD:

- AD progresses relentlessly (constantlty).
- 3 to 3.5 points decline on the MMSE/year.
- Mean survival ranges from three to eight years.

Pathology:

- Neurofibrillary tangles:

Paired helical filaments consisting of hyper-phosphorylated tau protein.
Found early in the entorhinal cortex, then hippocampus and temporal cortex

- Plaques:

extracellular loose aggregates of **amyloid** and preamyloid material

- Loss of neurons
- Granulovacuolar degeneration: intracytoplasmic vacuoles
- Amyloid angiopathy: in small and medium cortical and leptomeningeal arteries

Clinical cognitive assessment

- **Imaging:**

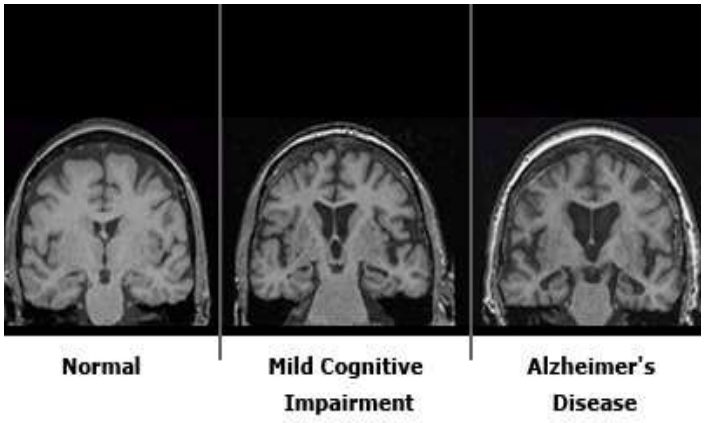
Hippocampal atrophy
R/O other pathologies

- **EEG:**

Diffuse background slowing

- **CSF:**

Increase tau



Treatment of AD

- **There is no cure**
- Modulate the course of the disease and/or ameliorate some symptoms
- Risk factors control
- Cognitive rehabilitation
- Treatment of associated symptoms: insomnia, depression, hallucinations, agitation
- Nutrition
- Aiming to slow the disease progression
- Mild-moderate:

Cholinesterase inhibitors (based on theory that there is selective loss of cholinergic cell bodies).
Donepezil, rivastigmine (available as patches), and galantamine.
Vitamin E (cardiotoxic)→ can cause or aggrevate heart failure

- Moderate-Severe (MMSE <17):

Add Memantine (N-Methyl-D-aspartate –NMDA- receptor blocker)→ NMDA receptor is a glutamate receptor

- Severe (MMSE <10)

Memantine
Palliative care

In Down syndrome patients, dementia occurs more frequently and at a younger age than in the general population. WHY?

Most people with Down syndrome have three copies of chromosome 21. This means that most people with Down syndrome have three copies of all genes coded on chromosome 21, while people without Down syndrome only have two copies. A specific brain protein called amyloid precursor protein (APP) is the protein that is thought to be associated with Alzheimer's disease. The gene that codes for APP is located on chromosome 21. Having three copies of the APP gene results in excessive production and depositing of the amyloid protein in the brain

#Vascular Dementia: (2nd most common cause of dementia)

- More common in males
- AD and VaD share risk factors
- Evidence of prominent executive dysfunction,
- Stroke history, vascular risk factors and high HachinskiIschemic Score* (>7)

Alzheimer Versus Vascular Dementia

Alzheimer	Vascular
Women	Men
Older age of onset	Younger than Alzheimer
Chromosome #21	Hypertension
Linear or progressive deterioration	Stepwise or patchy deterioration
No focal deficits	Focal deficits
Supportive treatment	Treat the underlying condition

*Hachinski Ischemic Score:

The Hachinski Ischaemic Score (HIS) represents a brief clinical tool helpful in the "bedside" differentiation of the commonest dementia types, Dementia of Alzheimer's Type (DAT) and Vascular Dememntia (VaD). It's utility has been validated by meta-analysis in pathologically verified patients with dementia. A cut-off score ≤ 4 for DAT and ≥ 7 for VaD has a sensitivity of 89% and a specificity of 89% (Moroney 1997). It is not useful in determinations between mixed dementia and other dementia types.

http://www.strokecenter.org/wp-content/uploads/2011/08/hachinski.pdf

#Lewy Body Dementia:

- Dementia, **psychosis**, extrapyramidal symptoms(Parkinsons)and fluctuation in attention.
- May have transient **lapses of consciousness.**
- More common in males.
- Pathologically charactarized by accumulation of Lewy bodies (eosinophilc inclusions).

#Frontotemporal Dementia:(=Picks disease)

- Rare.
- Onset in the 6th decade.
- 50% **familial.**
- **Poor judgment is the hallmark of the disease.**
- Suspect Frontotemporal Dementia with: early onset, more poor judgment than memory loss, aphasia.

How to differentiate causes of ireversible dementia?
Alzehimer Disease: Memory problems

Lewy body: Parkinsons + psychiatric "Hallucination" + lapses of consciousness

Frontotemporal Dementia: Familial + Poor judgment

→ in Alzehimer Disease there is global atrophy of the whole brain. It is not an atrophy of a specific part of the brain as you would see in Frontotemporal Disease. In Frontotemporal Disease, the atrohpy is in frontal and/or temporal lobe.

→ when you do Physical examination on Alzehimer Disease patients, you tend not to find focal deficits or neurological signs and symptoms. This is what differentiate Alzehimer Disease from vascular dementia where you find focal defecits and neurological signs and symptoms.. Ex: Right sided weakness, pseudobulbar palsy, dysphagia, dysarthria, abnormal reflexes.

Cases:

Case1:A 70 year-old man began crashing into the walls at night during violent dreams two to three nights per week. He had no cognitive or neurological impairment. A sleep study revealed RBD (REM sleep Behavior Disorder), which was successfully treated with low dose clonazepam. Six years later he developed mild cognitive symptoms and very mild Parkinsonian signs and seven years later he began seeing well-formed animals(=Hallucination).MMSE was 26 and clock drawing showed central placement of the numbers with mild micrographia. MOCA score was 18.

A diagnosis of Lewy Body Dementia (DLB) was made.

Treatmentwith acholinesterase inhibitor stabilized memory symptoms and decreased the frequency and intensity of visual hallucinations for 12 months. After the first year his cognitive, behavioral, and motor symptoms progressed gradually despite treatment.

The diagnosis of probable DLB requires dementia plus 2/3 of the following, Parkinsonism, well-formed visual hallucinations, and fluctuating alertness.

Executive and visuospatial deficits are often prominent in DLB and the MOCA is a more sensitive measure of cognitive impairment than the MMSE.

It is important to identify the target symptom, cognitive, behavioral, motor, or active sleep, when treating DLB. There is a prominent cholinergic deficit in patients with DLB and these patients often respond well to treatment with cholinesterase inhibitors. Patients with DLB may be sensitive to side effects of CNS medications, especially to neuroleptics. Low doses of CNS medications should be used with careful monitoring for side effects.

Case 2:A 55 year-old woman presented with gradual onset and progression of difficulty finding words and a change in behavior over one year. She was still working full time as a business executive and drivingwithout difficulty. She was more anxious and impatient and had decreased regard for the feelings of others. Her MMSE was 25 with **3/3 on delayed recall**.
3/3 on delayed recall→ means memory is perfect, so it is very unlikely to be AD
She had mild word finding difficulty and a normal sensorimotor exam. Her MRI revealed prominent temporal and frontal lobe atrophy. **Her mother had a progressive dementia beginning in her late fifties with a similar pattern of asymmetric atrophy on MRI**.
→ familial, meaning it is more likely Frontotemporal Disease.

Her mother's autopsy demonstrated Frontotemporal Disease, tau + Pick type. Genetic testing revealed a mutation in the tau gene on chromosome 17. Our patient experienced a steady decline in behavior and language over six years and now requires full-time care. Trials of cholinersterase inhibitors, memantine, and a number of medications to control behavioral symptoms were ineffective. No medications are currently approved to treat FTD but future trials are likely to target the primary pathology such as tau or progranulin.

Questions:

1. Which of the followings is **NOT** true for dementia?

a) Prevalence of dementia is about 5% among those over 65 years old.
b) Prevalence of dementia is about 20% in those over 80 years old.
c) A study in the UK revealed two-thirds of patients with dementia go unrecognized within the primary-care system.
d) Family physicians have an important role in identifying dementia in community.
e) Dementia involves only memory impairment while other cognitive functions are intact.

2. Which of the following is **NOT** an etiology of dementia?

a) Parkinson's Disease
b) Neurosyphilis
c) Creutzfeldt-Jakob Disease
d) HIV infection
e) Influenza infection

3. Which of the following is a typical feature of Alzheimer's Disease?

a) A stepwise deteriorating course.
b) A patchy distribution of neurological and neuropsychological deficits.
c) Fluctuating cognitive performance and degree of alertness.
d) Spontaneous motor features of parkinsonism.
e) Insidious in onset and gradual in progression.

4. Which of the following is **NOT** true about Acetylcholinesterase inhibitors (AChEIs)

a) Indicated in mild to moderate AD
b) Drug of choice for DLB
c) The main adverse effects seen are due to the cholinergic effect on the gastrointestinal tract.
d) Caution is warranted when prescribing AChEIs for those with significant bradycardia or cardiac conduction defects, prostatism, airways obstruction and peptic ulcer disease.
e) Can cure Alzheimer disease completely

Correct answer (All E)

Explanations:-

Q1 Dementia involves a **global mental impairment** compared with that individual's previous normal performance.

Q2 A stepwise deteriorating course and a patchy distribution of neurological and neuropsychological deficits should be features of vascular dementia. Fluctuating cognitive performance and degree of alertness, as well as spontaneous motor features of parkinsonism is suggestive of Dementia with Lewy bodies.

Q4 AChEIs are not considered as disease-modifying agents and do not alter the overall prognosis of AD. When response to an AChEI is eventually lost, patients usually decline quickly and lost any early benefit gained form the drug.