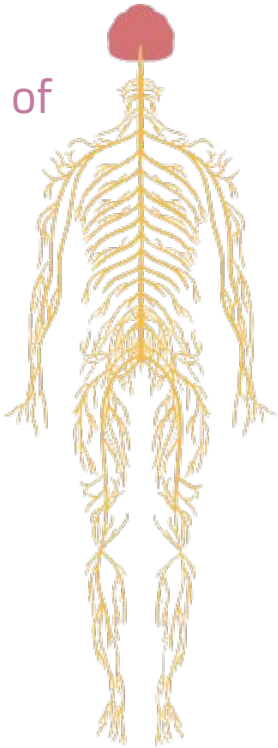
Introduction to degenerative brain diseases

Editing File

Color index :
Main text (black)
Female Slides (Pink)
Male Slides (Blue)
Important (Red)
Dr's note (Green)
Extra Info (Grey)

Objectives

- Explain the basic pathological concepts of neurodegenerative disease, using Alzheimer's and Parkinson disease as a classical example.
- Know the definition of "dementia" syndrome
- List the possible causes of dementia
- Understand the major clinic-pathological features of Alzheimer's disease
- Hypothesize the possible etiologies of Alzheimer's disease.
- List the causes of Parkinsonism
- Understand the major clinical and pathological feature of Parkinson disease



If you want to read the lecture from Robbins click here

FEMALES SLIDES

Degenerative Brain Diseases

Neurodegenerative diseases are characterized by the progressive loss of neurons, typically affecting groups of neurons with functional interconnections, rather than by the physical location in the brain.

They cause symptoms that depend on the pattern of involvement of the brain.
The term "Degenerative":
– an underlying cellular degeneration of neurons in the brain

Although many degenerative diseases have primary targets, other brain regions are often affected later in the course of the illness.

Diseases that involve the cerebral cortical neurons result in cognitive changes, often including disturbances of memory, behavior, and language. With time these progress to **dementia**, as occurs with Alzheimer disease.

Neurons of the basal ganglia result in movement disorders as with Parkinson disease.

Diseases that affect the cerebellum result in ataxia.

Diseases that affect the motor neurons result in weakness.

Dementia

01

It is defined as **the development of memory impairment and other cognitive deficits severe enough to decrease the affected person's capacity to function at the previous level despite /with preservation of a normal level of consciousness.**

02

It arises during the course of many neurodegenerative diseases; it also can accompany numerous other diseases that injure the cerebral cortex e.g. metabolic disorders, infections or toxins.

03

Dementia is an increasing public health concern as the population ages.
One of the most important public health issues in the industrialized world ,Dementia is a symptom, it's not a disease itself.

04

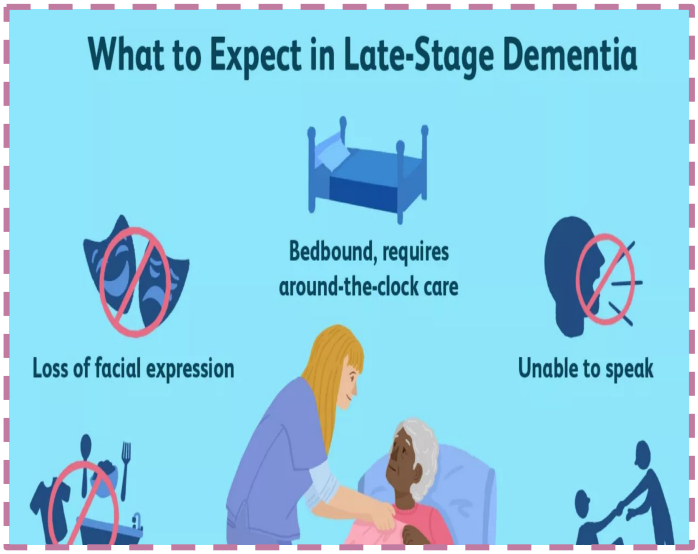
There are many causes of dementia, Regardless of etiology, dementia is not part of normal aging and always represents a pathologic process.

Deep Focus Question

Which of the following statements regarding dementia is true?

A. Dementia is part of normal brain aging.
B. Dementia is a sudden decline in memory.
C. Dementia is a progressive decline in brain functioning.
D. Dementia is never hereditary.

Answer: C



MALES SLIDES

Dementia

Major causes of dementia with examples

Primary Neurodegenerative Disorders

-Alzheimer disease
– Lewy body dementia
– Huntington disease

Infections

– Prion-associated disorders (e.g. Creutzfeldt-Jakob disease)
– HIV encephalopathy (AIDS dementia complex)
– Progressive multifocal leukoencephalopathy

Vascular and Traumatic Diseases

– Multi-infarct dementia
– Global hypoxic-ischemic brain injury
– Chronic subdural hematomas

Metabolic and Nutritional Diseases

– Thiamine deficiency (Wernicke-Korsakoff syndrome)

Miscellaneous

– Brain tumors
– Neuronal storage diseases
– Toxic injury (e.g. mercury)

Alzheimer Disease

Osmosis Vid

Definition

It is the most common cause of dementia in the elderly.
Dementia and parkinsonism are clinical syndromes but Alzheimer disease and Parkinson's disease are the neurodegenerative disease

While Alzheimer's disease is considered as "degenerative"-that is, reflecting an underlying cellular degeneration of neurons in the brain- not all forms of dementia are degenerative

Epidemiology

When considered by age groups, the incidence of Alzheimer disease:

- 3% for individuals 65 to 74 years old
- 19% for individuals 75 to 84 years old
- 47% for individuals 85 years old or more

This increasing incidence with age has given rise to major medical, social, and economic problems in countries with a growing number of elderly

Alzheimer Disease

Clinical features

Early manifestations

- The disease usually manifests with the\ becomes clinically apparent as insidious onset of impairment of higher intellectual function, with alterations in\ **memory impairment**, and altered mood and behavior

Late manifestations:

– severe cortical dysfunction occurs with progressive disorientation, memory loss and aphasia (inability to speech)

-Over the next 5 to 10 years, the patient becomes profoundly disabled, mute, and immobile. Death usually occurs from intercurrent pneumonia or other infections due to prolonged time in bed

Etiology

Most cases are sporadic (not familial/hereditary). At least 5% to 10% are familial.

In general, patients rarely become symptomatic before the age of 50, but early onset can be seen with some of the heritable forms.

Evidence from familial forms of the disease indicates that the accumulation of a peptide (β amyloid, or Aβ) in the brain initiates a chain of events that result in the morphologic changes of Alzheimer disease and dementia

FEMALES SLIDES

Alzheimer Disease Pathogenesis

The fundamental abnormality in AD is the accumulation of two proteins (Aβ and tau) in specific brain regions, in the forms of plaques and tangles, respectively. The anatomic distribution of these changes, which occur roughly in parallel, are responsible for the clinical signs and symptoms; they appear to develop well in advance of clinical presentation

1-plaques:

1

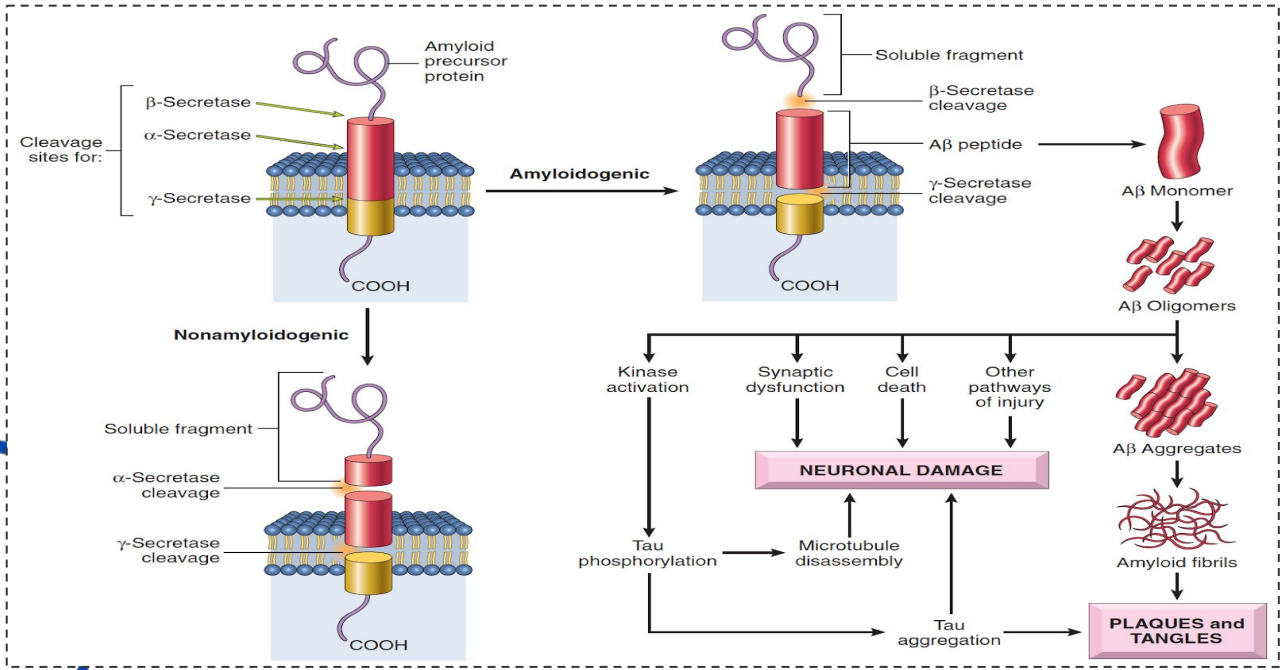
Plaques are deposits of aggregated Aβ peptides in the neuropil, (any area in the nervous system composed of mostly unmyelinated axons, dendrites and glial cell processes that forms a synaptically dense region containing a relatively low number of cell bodies)

Aβ generation is the critical initiating event for the development of AD. Aβ is created when the transmembrane protein amyloid precursor protein (APP) is sequentially cleaved by the enzymes **β-amyloid–converting enzyme (BACE) and γ-secretase.**

2

3

APP also can be cleaved by α-secretase and γ- secretase, liberating a different peptide that is nonpathogenic.
The generation and accumulation of Aβ occur slowly with advancing age.



Alzheimer Disease Pathogenesis

cont plaques:

Amyloid precursor protein cleavage by α-secretase and γ-secretase produces a harmless soluble peptide (non pathogenic), whereas amyloid precursor protein cleavage by β-amyloid–converting enzyme (BACE)and γ-secretase releases Aβ peptides, which form pathogenic aggregates and contribute to the characteristic plaques and tangles of Alzheimer's disease.

The search for genes associated with typical, sporadic AD is beginning to identify genetic associations that may provide new clues about the pathogenesis of the disease.

Effects of accumulated Aβ on neurons and neuronal function

Small aggregates:

- ❖ Alter neurotransmission -(inhibit electrical transport through the neurons)
- ❖ Aggregates can be toxic to neurons and synaptic endings

Larger deposits, in the form of plaques:

- ❖ Lead to neuronal death
- ❖ Elicit a local inflammatory response that can result in further cell injury
- ❖ May cause altered region-to-region communication through mechanical effects on axons and dendrites.

Alzheimer Disease Pathogenesis

2-Tangles :

tangles are aggregates of the microtubule binding protein tau, which develop, intracellularly and then persist extracellularly after neuronal death.

Mechanism of tau protein is not completely understood but thought that the presence of Aβ leads neurons to activate Kinase enzyme causing **hyperphosphorylation of the microtubule binding protein "tau"** resulting in the loss of its ability to bind to microtubules. This process also results in neuronal dysfunction and cell death.

The anatomic distribution of these changes, which occur roughly in parallel, are responsible for the clinical signs and symptoms; they appear to develop well in advance of clinical presentation

Extra INFO

Just like any other cell, neurons are held together by a cytoskeleton giving the cell its shape, offers support and facilitates movement through 3 main components: microfilaments, intermediate filaments and microtubules. Tau protein is an abundant protein in nerve cells performing the of function of stabilizing microtubules. #med437

Extra

To make sure you understood the pathogenesis!

The cause of Alzheimer disease isn't completely understood but there are two major factors
that play arole:
A- Plaques:
In the neuronal cell membrane there is a protein called amyloid precursor protein (APP) which
play a role in neuron growth and repair (normal protein). and like any other protein it will be
used then cleaved. APP has 2 pathways.

1- APP will be cleaved by alpha secretase and gamma secretase which will form a soluble complex that the body can get rid of and won't be accumulated (normal pathway).

2- APP will be cleaved by beta secretase and gamma secretase which will form the beta amyloid (A beta) => => when more are formed it accumulates, becomes toxic and interferes
with function of neuron and disrupts signaling => as they increase they form insoluble complex that the body cannot get rid of => forming Beta amyloid PLAQUES* extracellular (abnormal pathway)

* Beta plaques are beta amyloid proteins accumulated and formed plaques
* SO TO SUM UP : beta secretase => the enzyme which forms Beta amyloid from APP that causes Alzheimer's.

B- Tangles:
Inside the cell there is a protein called tau which is present in the microtubules and makes sure it doesn't break apart. somehow the formation of A beta plaques initiate hyperphosphorylation of tau protein => aggregation of hyperphosphorylated tau protein inside the cell " neurofibrillary tangle"

Pathological hallmarks of Alzheimer disease include "positive" lesions such as amyloid plaques and cerebral amyloid angiopathy, neurofibrillary tangles.

Alzheimer Disease

Forms of Alzheimer

Sporadic form (most cases, 90-95%)	Familial form (5-10%) of cases
Late onset Early onset	early onset (Due to Inheritance of a dominant gene speeding up progression of the disease)
1- Early onset | **(ApoE4)** ε4 , An allele of apolipoprotein: - May contribute to the deposition of Aβ, but how it does so is not known. - Associated with as many as 30% of cases. - it is thought to both increase the risk and lower the age of onset of the disease. 2- Late onset | **SORL1** gene: - Also recently been found to be associated with late-onset Alzheimer disease - Deficiency of the SORL1 protein may alter the intracellular trafficking of APP, shuttling it to a compartment where the Aβ peptide is generated by enzymatic cleavage, the net result being increased generation of Aβ (pathogenic peptide)	1- Mutations in APP or in components of γ-secretase (presenilin-1 or presenilin-2) lead to early onset familial Alzheimer disease by increasing the rate at which Aβ accumulates \ is generated - PSEN-1 gene (on chromosome 14) which encode for presenilin-1 - PSEN-2 gene (on chromosome 1) which encode for presenilin-2 2- Down syndrome (trisomy 21) *extra chromosome 21): - APP gene is found on chromosome 21, meaning that patients with down syndrome have an extra APP gene, therefore AD occurs in almost all patients with Down syndrome who survive beyond 45 years of age due to APP gene dosage effect

Diagnosis

- Although pathologic examination of brain tissue remains necessary for the definitive diagnosis of Alzheimer disease, the combination of clinical assessment and modern radiologic methods allows accurate diagnosis in 80% to 90% of cases
- Because these may also be present to a lesser extent in the brains of elderly nondemented individuals, the current criteria for a diagnosis of Alzheimer disease are based on a combination of clinical and pathologic features

Pathological Features of alzheimer Neuritic plaques

Overview

- Plaques (a type of extracellular lesion) and neurofibrillary tangles (a type of intracellular lesion) may be present to a lesser extent in the brains of elderly nondemented individuals, therefore the current criteria for diagnosis of AD is based on a combination of clinical and pathological features.
- There is a fairly constant pattern of progression of involvement of the brain regions pathologic changes: The earliest occur in the entorhinal cortex → then spread through the hippocampal formation and isocortex →extend into the neocortex.
- Silver staining methods or immunohistochemistry are extremely helpful in assessing the true burden of these changes in a brain.

Microscopic

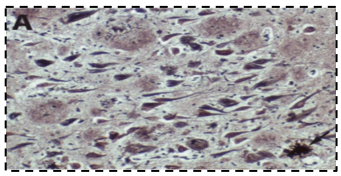
Focal , spherical collection of dilated tortuous, silver-staining neuritic processes (dystrophic neurites) often around a central amyloid core which contain Aβ

Plaques can be found in the hippocampus and amygdala as well as in the neocortex, although there is usually relative sparing of primary motor and sensory cortices until late in the course of the disease.

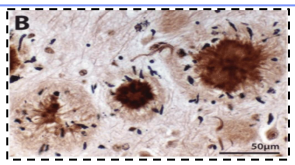
Aβ deposits can also be found lack any surrounding neuritic reaction termed diffuse plaques.

Silver staining of cortical brain tissue showing:

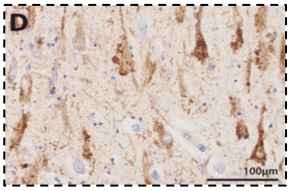
Showing plaques and tangles in the cortex and higher power image of silver positive neuritic plaques.



Amyloid-beta protein in the plaques

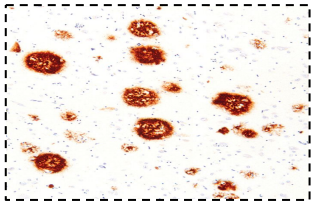


Scale in C (tau next page) equivalent toA. Arrows indicate neuritic plaques.



Immunohistochemical stain

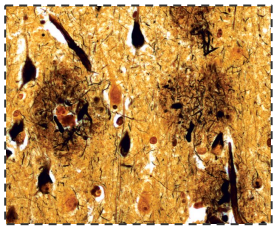
Immunohistochemical stain for Aβ. Peptide is present in the core of the plaques (circle) as well as in the surrounding region.



Bielschowsky stain

Plaques (arrow) contain a central core of amyloid and a surrounding region of dystrophic neurites (Bielschowsky stain)

Dendrites (neuritic not diffuse plaques)



FEMALES SLIDES

Pathological Features of alzheimer Neurofibrillary Tangles

Microscopic

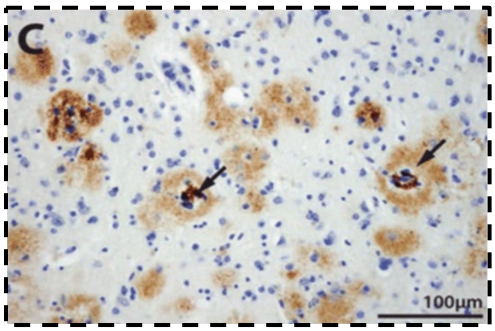
Bundles of Paired helical filaments, visible as basophilic Fibrillary structures in the cytoplasm of neurons that displace or encircle the nucleus .

Tangles is (a type of intracellular lesion) Cytoplasmic, until the cell dies then become extracellular (Displace or encircle the nucleus).

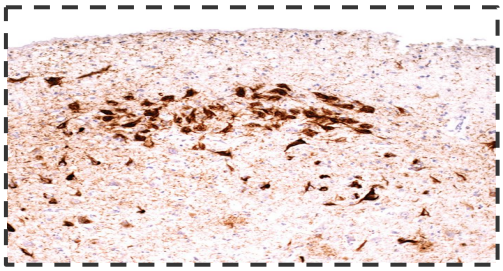
A major component of paired helical filament is abnormal hyperphosphorylated forms of the protein tau

Tangles are no specific to alzheimer disease , being found in other degenerative disease as well

They are commonly Found in :
-cortical neuron especially in Entorhinal cortex
-Pyramidal cells of hippocampus
-Amygdala
-Basal forebrain



Hyperphosphorylated tau in tangles (silver staining)

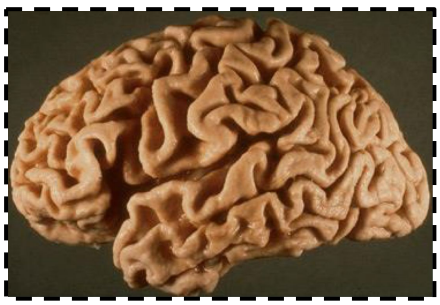


Neurons containing tangles stained with an antibody specific for tau.

Macroscopic

A variable degree of cortical atrophy with widening of the cerebral sulci that is most pronounced in the frontal, temporal, and parietal lobes

With significant atrophy, there is compensatory ventricular enlargement (hydrocephalus ex vacuo)



Parkinsonism

Definition

Parkinsonism is motor disturbance that is seen in a number of conditions \ range of diseases that share **damage to dopaminergic neurons of the substantia** Nigra or their projection to the striatum, related to control of movements. Parkinsonism is a clinical syndrome characterized by tremor, rigidity, bradykinesia, and instability.

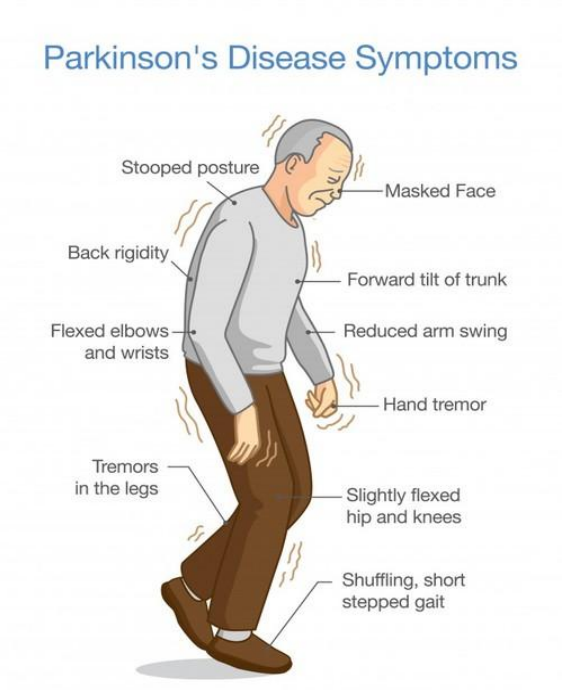
Etiology

- **Idiopathic**: ex. **Parkinson disease** (most common neurodegenerative disease associated with parkinsonism)
- Drug-induced: Drugs that affect these neurons, particularly dopamine antagonists and toxins.
- Other neurodegenerative diseases: ex. Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) and Corticobasal Degeneration (CBD)
- Infections: ex. Post-encephalitic parkinsonism (associated with the influenza pandemic)
- Rare: Head trauma, Stroke

Clinical Features

IMPORTANT

- diminished facial expression (**masked face**)
- **stooped posture**
- -**slowness of voluntary movement**(**Bradykinesia**)
  -Festinating gait(progressively shortened,accelerated steps)
- **Pill-rolling tremor** (كأن معه مسبحة)
- Rigidity & instability(Cogwheel rigidity, major sign of parkinson disease)



Parkinson's Disease

Osmosis Vid

Epidemiology

It occurs in the 6th to 8th decades.

It affects more than 2% in North America ,Develop disease

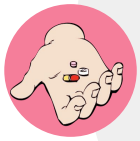
It affects men more than women.

The crude prevalence rate in Saudi population if 22/100,000.

Diagnosis

Progressive parkinsonism.

Absence of a toxic or other known underlying etiology (**idiopathic**).



Clinical response to (L-dihydroxyphenylalanine **L-DOPA**) treatment

Parkinson Disease

Pathogenesis

- While most Parkinson disease is sporadic, there are both autosomal dominant and recessive forms of the disease
- Genetic analysis has identified specific causal mutations, For example;
  - α-synuclein mutations cause autosomal dominant Parkinson disease
  - as can gene duplications and triplications
- Point mutations and duplications of the gene encoding α- synuclein, a protein involved in synaptic transmission, cause autosomal dominant PD.

- Even in cases of Parkinson disease not caused by mutations in this gene, the **diagnostic feature of the parkinson disease**-the Lewy body-is an inclusion containing **α-synuclein**, a widely expressed neuronal protein that is involved in synaptic transmission and other cellular processes.
- The Pathological hallmark of the disease is the appearance of Lewy bodies.
- How the alterations in sequence or protein levels result in disease is **unclear**.
- The presence of α-synuclein in Lewy bodies has suggested that **defective degradation** of the protein in the proteasome might play a role.
- **This is supported by the identification of two other genetic loci for Parkinson disease**:

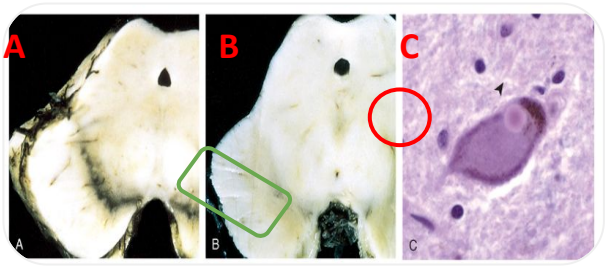
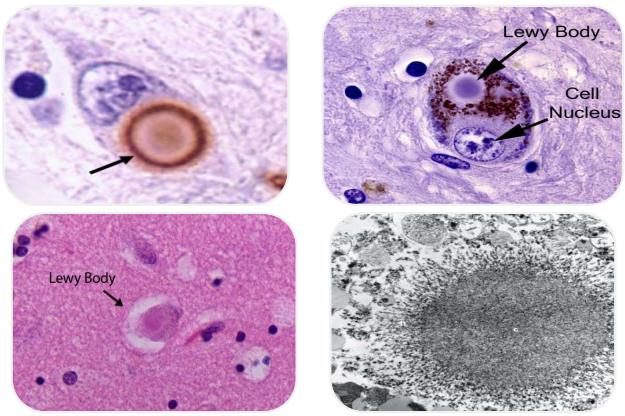
1- Loci which involve genes encoding parkin (an E3 ubiquitin ligase)

2- UCHL-1 (an enzyme involved in recovery of ubiquitin from proteins targeted to the proteasome

Clinical Note

- Rare cases are due to inherited mutations in PARK1 on chromosome 4 which encodes A -synuclein, a component of Lewy bodies.
- Note that parkinsonism is not specific to Parkinson's disease; it merely reflects a dysfunction of the substantia nigra system. Other causes of parkinsonism include drugs, toxins, infections, and trauma.
- Patients present with Tremor, rigidity, and bradykinesia (parkinsonism).

Parkinson Disease

Macroscopic	Microscopic
Pallor and depigmentation of the substantia nigra pars compacta and locus coeruleus	loss of the pigmented, neurons in these regions
-	associated with gliosis
 (A) Normal substantia nigra. (B) Depigmented substantia nigra in idiopathic Parkinson disease. (C) Lewy body in a neuron from the substantia nigra stains pink.	Lewy bodies may be found in some of the remaining neurons 

Lewy Bodies

Osmosis Vid

1. Single or multiple, intracytoplasmic, eosinophilic, round to elongated inclusions that often have a dense core surrounded by a pale halo.
2. Ultrastructurally, Lewy bodies are composed of fine filaments, densely packed in the core but loose at the rim
3. These filaments are composed of α-synuclein, along with other proteins, including neurofilaments and ubiquitin.
4. The other major histologic finding is Lewy neurites (dystrophic neurites) that also contain abnormally aggregated α-synuclein.

Parkinson Disease

Treatment

L-DOPA therapy is often extremely effective in symptomatic treatment, but it does not alter the progressive nature of the disease.

Over time, L-DOPA becomes less effective at providing the patient with symptomatic relief and begins to cause fluctuations in motor function on its own.

Current neurosurgical approaches to Parkinson disease include the placement of lesions in the extrapyramidal system to compensate for the loss of nigrostriatal function or placement of stimulating electrodes - deep brain stimulation.

Prognosis and hallmarks

1

It usually progresses over 10 to 15 years.

There is an eventual severe motor slowing to the point of near immobility.

2

3

Death is usually the result of intercurrent infection (Usually pneumonia) or trauma from frequent falls caused by postural instability.

About 10% to 15% of individuals with Parkinson disease develop dementia (At the end of the disease),with the incidence increasing with advancing age.

4

Parkinson Disease

Dementia in Parkinson's

01

Course

The characteristic feature of this disorder includes a fluctuating course and hallucinations.

02

Dementia

While many affected individuals also have pathologic evidence of Alzheimer disease, the dementia in other Parkinson disease patients is attributed to widely disseminated Lewy bodies in the cerebral cortex.

03

Lewy bodies

When dementia arises within 1 year of the onset of motor symptoms, it is Lewy bodies dementia

Take Home Messages

FEMALES SLIDES

- Neurodegenerative diseases cause symptoms that depend on the pattern of involvement of the brain.
- Diseases that affect the cerebral cortex primarily (e.g. Alzheimer's disease) are more likely to cause cognitive change, alterations in personality and memory disturbance.
- Accumulation of the Abeta peptide, derived from amyloid precursor protein, is central to the pathogenesis of Alzheimer's disease.
- Dementia is a non-specific illness syndrome that has many causes.
- Diseases that affect the basal ganglia(e.g. Parkinson's disease) have motor symptoms as prominent clinical features.
- Parkinsonism is not parkinson's disease.
- Parkinson's disease is associated with abnormal aggregation of proteins, which may lead to
- loss of function or may trigger apoptosis.familial forms are associated with ,mutations in the genes encoding these proteins.

Keywords

Alzheimer	• impaired intellectual function • memory impairment • aphasia • Plaques : Extracellular , aggregated Aβ peptides • Normal cleavage by : α-secretase and γ-secretase • Abnormal Cleavage : β-amyloid–converting enzyme and γ-secretase • Tangles: mainly intracellular & could be extracellularly , Tau Accumulation • hyperphosphorylation of microtubule binding protein Tau • cortical atrophy • widening of sulci • hydrocephalus ex. vacuo
Parkinson	• α-synuclein mutations & accumulation • Lewy bodies dementia • Response to L dopa • Pallor substantia nigra pars compacta & locus coeruleus • Tremor • Dysarthria • Akinesia • Shuffling gait • Rigidity • Pin rolling tremor at rest
	Lewy body : • dense core surrounded by a pale halo. • composed of α-synuclein

MCQ

A 64 years old male patient with DM present with tremor , dysarthria and akinesia which of the following structures is most likely affected?

A- Thalamus

B- Substantia nigra

C- Corpus callosum

D- Limbic system

Daughter of a patient complaining that her 70 years old mother became forgetful, loses her keys, has memory problems. What do you expect to find microscopically?

A-Neuritic plaque

B- Lewy bodies

C- Red neurons

D- Loss of myelin

Abnormalities in which of the following will lead to the creation of neurofibrillary tangles?

A- Tau protein

B- Amyloid precursor protein

C- Neutrophils

D- Mitochondria

Which one of the following is accumulated in Parkinson's?

A- Alpha-synuclein

B- Amyloid precursor protein

C- Antitrypsin

D- TDP 43

1- B/ 2-A / 3-A / 4-A

MCQ

Which ONE of the following enzyme cleavage sequences would lead to Aβ production from the amyloid precursor protein?

A- α-secretase and then γ-secretase

B- β-secretase and then γ-secretase

C- γ-secretase and then α-secretase

D- γ-secretase and then β-secretase

The classical histopathological finding in alzheimer's disease is?

A-Rosenthal fibers

B- Astrocyte with gliosis

C- Neurofibrillary tangles

D- Lewy bodies

A 80 year old woman has a stooped posture, masked face and a pill-rolling tremor that have been present for the last five years. Which of the following will be seen in the brain in large numbers?

A-Senile plaque

B- Lewy bodies

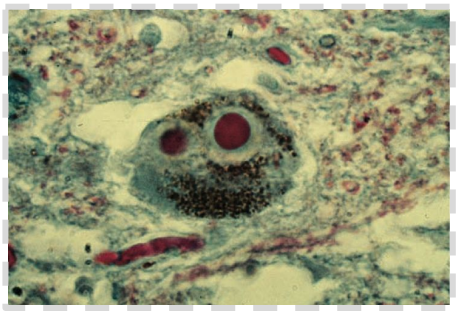
C- Neurofibrillary tangle

D- Dopaminergic neurons

Need a SUMMARY ? Click here

1-B / 2-C / 3-B

Cases

1.A 76-year-old man is admitted to the hospital for evaluation of progressive memory loss and disorientation. The pupils are small but react normally to light. Muscle tone is normal. A lumbar puncture returns clear, colorless CSF under normal pressure. An electroencephalogram shows diffuse slowing. A CT scan of the brain reveals moderate atrophy. Which of the following is the most likely diagnosis?			
A.Alzheimer disease	B.Creutzfeldt-Jakob disease	C.Glioblastoma multiforme	D.Huntington disease
2.An 88-year-old woman with Alzheimer disease dies of congestive heart failure. Examination of the brain at autopsy shows bilateral atrophy of the gyri, particularly in the frontal and hippocampal cortex. What additional finding might be expected in the brain of this patient?			
A.Cerebritis	B.Hydrocephalus ex vacuo	C.Lissencephaly	D.Pachygyria
3.A 68-year-old woman complains of difficulty getting out of a chair. On examination, the patient shows reduced facial expression, a resting tremor, cogwheel rigidity, and bradykinesia (slowness of voluntary movements). The patient dies of congestive heart failure 10 years later. Microscopic examination of brain tissue at autopsy is shown in the image. The spherical, eosinophilic inclusions in the cytoplasm of this pigmented neuron are composed of which of the following proteins? 			
A.b-Amyloid	B.Polyglutamine	C.a-Synuclein	D.Tau
4.A 35-year-old man with Down syndrome dies of acute lymphoblastic leukemia. Gross examination of the patient's brain at autopsy shows mild microcephaly and underdevelopment of the superior temporal gyri. Histologic examination would most likely show which of the following neuropathologic changes?			
A.Lewy bodies	B.Negri bodies	C.Neurofibrillary tangles	D. AA amyloidosis

1-A / 2-B / 3-C / 4-C

NEED EXPLANATION ? CLICK HERE

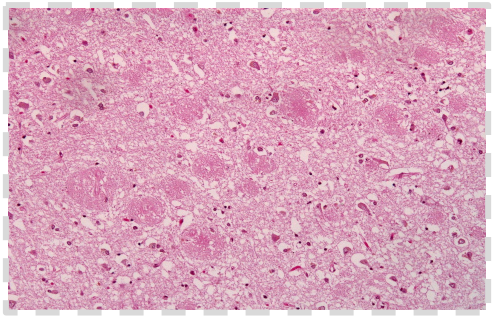
Cases

EXTRA CASES REQUIRE EXTRA INFO

1.A 77-year-old man is brought to the clinic by his son due to an "inability to take care of himself." The patient is unable to prepare food, bathe himself, or take daily medications. According to the son, his father has had difficulty remembering recent events, such as his grandson's birthday party last month, but he is able to recall events that occurred many years ago, such as his own wedding. Eight months ago, the patient was forced to give up driving after he got lost in his own neighborhood on numerous occasions. Which of the following pathologic findings is most likely to be present within the neurons of this patient's brain?

A.Alpha-synuclein-positive cytoplasmic inclusions	B.Brownish-yellow granular material composed of lipid and protein	C.Round eosinophilic cytoplasmic inclusions due to viral infection	D.Hyperphosphorylated microtubule-associated proteins

2.A pathologist is examining brain biopsies from a patient who died from a neurodegenerative condition following an episode of aspiration pneumonia. A tissue sample from the patient is demonstrated :
Further staining reveals patchy red plaques that become yellow when viewed under polarized light . Which of the following clinical courses was most likely seen in this patient?



A.Mild decline in cognitive functioning	B.Early memory loss followed by behavioral changes	C.Stepwise deterioration in cognition	D. Seizures

3.A 65-year-old man comes to the office escorted by his partner due to recent falls and confusion. Additionally, the partner states that multiple times throughout the night, the patient exhibits various movements in his sleep, such as throwing a ball and even accidentally kicking her one night. The patient states he is unaware of these activities, but he describes vivid dreams of playing football or fighting off home invaders. The patient's partner mentions that the symptoms began a year ago, and since then, they have been getting worse, although some days are better than others. Medical history is unremarkable. Vitals are within normal limits. Physical examination reveals muscle rigidity in the upper extremities, and the patient walks slowly with small steps. On Mini-Mental State Examination the patient has difficulty with copying overlapping pentagons and drawing a clock but can repeat 3 objects after 1 and 5 minutes respectively. Which of the following is the most likely diagnosis?

A.Frontotemporal dementia	B.Alzheimer disease	C.Dementia with Lewy bodies	D.Normal-pressure hydrocephalus

1-D / 2-B / 3-C

PATHOLOGY TEAM

Leader زياد العتيبي

- عبدالله الكودري
- رند ابا الخيل
- ساره العجاجي
- نوره المحيميد
- فيصل الشويعر
- رغد المصلح
- عروب المحمود
- يزيد ال طلحه
- سلطان البقمي
- رزان السطيحي

Leader لمى العتيبي

- شوق الخليفة
- محمد العرفج
- ريما المطيري
- وعد العنزي
- منصور العتيبي
- معاذ الحضيف
- الحوراء العوامي
- لؤي الحديثي
- يزيد المطيري

- هياء العجمي
- عمر المقرن
- محمد معشي
- أفنان الأحمري
- عائشة ابراهيم
- ريماز المحمود
- ليان الرويلي
- نوره المالك
- الجوهرة الوهيبي

CONTACT US :
Pathologyteam443@gmail.com