

CNS PATHOLOGY

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Malformations

-Etiology of CNS malformations remain unknown.

-Is thought to be caused by genetic factors, infectious agents (e.g. TORSH), toxic compounds/ drugs.
Chemical material

Neural tube defect

-The most common CNS malformation.

-Midline anomalies that involve neural tissue, meninges, and overlying bone or soft tissue.

-Pathogenesis and Morphology: 2 forms
(primary)

1. Failure of neural tube closure at 28 days of gestation >> secondary mesenchymal tissue defects around the malformed tube. e.g.,
and bone tissue

*Anencephaly: absence of most of the brain and skull.
supra tentorial *بقايا الدماغ فوق الجافية* *or بقايا الدماغ* *من الدماغ* *[خلفه]*

*Meningo(myelo)cele: the soft tissue open and out protruding of meninges + nervous tissue
thin layer of skin *مغطى*
=protrusion of meninges and spinal cord through a vertebral defect.

=Meningocele: only a meningeal protrusion through a vertebral defect. no nervous tissue

=most commonly in the lumbosacral region. *voluntary*
Autonomous *→ incontinence*

=motor and sensory deficits in the lower extremities.

=disturbances of bowel and bladder control.

=superimposed infection of the cord due to defective barrier of the thin overlying skin.
due to open *↑ incidence* *[serious ↑ mortality rate]*

2. Primary bony defects >> secondary CNS abnormalities e.g.,

*Encephalocele: protrusion of malformed brain tissue through a midline defect in the cranium, most commonly occurs in the occiput, sometimes in nasofrontal area.
in the midline of occiput area usually / frontal area sometimes

*Meningocele. no nerve tissue structure.
→ frontal lobe

*Spina bifida: the most common neural tube defects, may be asymptomatic vertebral defect (spina bifida occulta) or severe, associated with meningeal outpouching through the vertebral defect.
need special technique to see it

-Microscopy: disorganized glial or neural tissue with choroid plexus.

micro circulation consist of:- arterials, capillary structure, venules in cardiovascular system..

Cerebral edema

hydrostatic press.

osmotic P.

G in BV called oncotic P. [H.P.]

system..

to do the gas change

serous.

-The ICP rises in these clinical settings: cerebral edema, increased CSF volume, and focally expanding mass lesions. edema accumulation of fluid in the ECS...

↳ most freq. cause.

-Cerebral edema: is the result of increased fluid leakage from blood vessels and injury to various cells of the CNS. (CNS lacks lymphatics hence it is easier for fluid to accumulate).

inside nervous system there is no lymphatic system → more sensitive to edema..

-Pathways:

1. Vasogenic edema

vascular system

*Blood-brain barrier disruption >> increased vascular permeability >> is an increase in extracellular fluid.

*The paucity of lymphatics >> impairs the resorption of excess extracellular fluid.

*May be either localized (inflammation or neoplasms), or generalized (following a global ischemic injury).

local Ischemia

if there is tumor around it there is edema

- generalized symptoms
- " edema.

2. Cytotoxic edema

↳ cell injury

*Due to generalized hypoxia/ ischemia or a metabolic derangement >>

neuronal/glia/endothelial cell membrane injury >> increase in intracellular fluid.

influx of fluid inside the cell

*Generalized edema often involve both vasogenic and cytotoxic edema.

Hydrocephalus

↑CSF

-Accumulation of excessive CSF within the ventricular system.

-Most cases are related to impaired flow or reduced resorption.

-Rarely >> overproduction by choroid plexus tumors (the most common one: choroid plexus papilloma).

↑CSF

↓ rare

-Increased volume of CSF >> expands the ventricles >> elevate the ICP.

-In infancy (before closure of the cranial sutures) >> the head enlarges.

-2 types

*Obstructive (non-communicating): obstruction in the ventricular system.

*Communicating: no obstruction.

↳ in the junction between intra ventricular and subarachnoid spaces..

Choroid plexus

infection, meningitis → the subarachnoid infected and damaged granulation.

absorption of CSF

aggregation of ependymal cell + vascular strat.

The choroid plexus within the ventricular system produces CSF which circulates through the ventricular system then enter the Subarachnoid space through the foramina of Luschka and Magendie then absorbed by arachnoid granulations.

absorption of CSF via granulation.

CSF

Raised ICP and herniation

Raised ICP and herniation

Herniation is the displacement of brain tissue through falx and tentorium or openings in the skull (e.g. foramen magnum) because of increase ICP. → قد يفصله نكريه اجزائه

- Mostly caused by mass effects.

-Elevated ICP may also compress the vasculature and reduce perfusion of the brain >> ischemic injury and exacerbating edema. $\propto$ hydrostatic P. in the arterial system and inside the tissue

↳ lead to edema.

-Morphology: → pass below the falx cerebri

***Subfalcine (cingulate) herniation**: **unilateral expansion** of a cerebral hemisphere displaces the cingulate gyrus under the falx >> compression of the **ACA**. → *Ischemia*

***Transtentorial herniation:** medial aspect of the temporal lobe is compressed against the free margin of the tentorium >> compression of **CN III, PCA, and Contralateral cerebral peduncle, duret hemorrhages** (secondary hemorrhagic lesions in the midbrain and pons).

* **Tonsillar herniation**: displacement of the cerebellar tonsils through the foramen magnum
 >> brainstem compression and compromises vital respiratory and cardiac centers in the medulla.
part of cerebellum pass through foramen magnum

Neurodegenerative diseases

- Disorders characterized by the progressive loss of particular groups of neurons with shared functions.

* البروتين ← تتكون من AA على ال DNA فصل و foldation (فصل ، التقاط لل AA على البروتين) فتشكل البروتين ثم لا بد انه لا تخلف

*Due to mutations: Alter conformation, processing or clearance of the protein. end by expose some site + disappear other sites

* Imbalance between synthesis and clearance (protein itself is normal): Related to **genetic**, environmental and stochastic factors. مع خلل عند الـ AA علاج متعلق بعوامل وراثية خارج يتم إدارته بالشكل الصحيح

-Additional protein aggregation: neuron سبب تراکمی اور اعصاب متلاطم اور

*More and more protein aggregate >> the normal function of the protein is lost >> cell injury. ← إلى شدة الحد التي يتغير بآلية degradation resistant " + تتراكم بروتين غير typical وضعه التخلع منه

*Protein aggregates behave like **prions**: aggregates derived from one cell may be taken up by another, can spread from one site in the brain to another, transmissible between individuals (only the classic prion diseases). ← لنقل ال aggregation عن طريق العقل راجع يبعد

called / spongotic encephalopathy:- لحم فانتون {
-Not transmissible. ميكروسكوبية Brain tissue

-Inclusions seen in IHC.

→ the small aggregate :- more toxic

more destructive effect

* but the huge, large aggreg.

← غير قاررة على انتقال النور
less toxic

Alzheimer disease

-Neurodegenerative disease.

-The most common cause of dementia in older adults.

-Impairment of higher cognitive functions.

-Deficits in (over a course of 5-10 years): Memory, Visuospatial orientation, Personality, Language.

-Becomes profoundly disabled, mute and immobile.

-40% for 85-89 YO, 5-10% are familial.

-Pathogenesis:

* Accumulation of 2 proteins:

=Aβ: Critical initiating event. =Tau: Insufficient to induce Aβ deposition.

* As a result of excessive production and defective removal.

* In specific brain lesion.

* 2 hallmarks (Both contribute to neuron dysfunction)

=Amyloid plaques: deposits of the aggregated Aβ in the neuropil.

=Neurofibrillary tangles: aggregates of tau (microtubule binding protein), persist after death.

-Morphology:

* Cortical atrophy: Cortex is thinner.

=Thickness of gyrus is reduced + sulcus widening.

=Mainly the medial part of temporal lobe (hippocampus, entorhinal cortex, and amigdala).

=Sparing of primary motor and sensory cortices.

* Compensatory ventricular enlargement.

* Neuritic plaques: abnormal.

=Focal, spherical collections of dilated, tortuous, axonal or dendritic processes (dystrophic neurites) around a central amyloid core (mainly Aβ; a peptide derived by proteolytic cleavage of APP, may also contain tau aggregates).

=Microglial cells and reactive astrocytes are present at their periphery.

* Neurofibrillary tangles:

=Tau-containing bundle.

* familial: Genetic disease
* Congenital: Inborn with genetic defect
* hereditary: Genetic defect passed from parent to child

المرض خاضعاً

عند الإصابة به هو مرض

أو Tau بغيره كسبب الازهاق

amyloid precursor protein (APP) transmembrane protein around the synapse
Aβ is a small peptide derived from APP
eosinophilic hematoxylin material

fibrillary background

* generalized in the Brain.

* primary motor and sensory cortex are relatively spared.
Late

^{the Tan}
=Displace or encircle the nucleus.

=Have an elongated "flame" shape in pyramidal neurons.

=Rounded contour ("globose" tangles).

=Basophilic fibrillary structures with H&E staining, more clearly by silver staining and IHC.

^{degenerative} =Insoluble and resistant to clearance in vivo >> remaining visible in tissue sections as "ghost" or "tombstone" tangles after neuron death.

=In contrast to neuritic plaques, neurofibrillary tangles are non-specific for AD.

Parkinson's disease

-Neurodegenerative disease.

-Hypokinetic movement disorder.

-Caused by Loss of dopaminergic neurons from the substantia nigra >> reduction of dopamine in the striatum.

-Clinical: we don't make Brain stem Biopsy...

*Masked faces no face expression.

*Stooped posture

*Festinating gait *Rigidity

*"Pill-rolling" tremor

-Diagnosis is based on the triad:

*Tremor

*Rigidity

*Bradykinesia

*Absence of toxic etiologies

*Response to L-DOPA replacement therapy

-Morphology

*Pallor of the substantia nigra

*Lewy bodies: remaining neurons multiple cytoplasmic eosinophils or single

=In some of the remaining neurons.

=Single or multiple cytoplasmic eosinophilic.

=Round to elongated inclusions.

→ not specific for Alzheimer disease.

قد يظهر بأشكال أخرى من neurodegenerative diseases.

dark color

لأنه يخرج من tract لا striatum فيخرج حتمياً
هذا البروتين هناك

كل خطوة يكون ال amplitude → الخطوات تكون رصاصة / ضلوع الحصى
تتبعها أختل من بعد + أرتج ..

لهب فتح الذراع منه
بعض

بشرط عدم وجود
any toxic effect..

يتحسن بسرعة مع هذا الدواء

← ولكن مع الوقت يصبح يحتاج dose أعلى
منقل أو يحتاج لهذا العلاج ...

تصبغ white

[cytoplasmic center surrounded by clear
halo in some of remaining neurons].