Lecture One

Cellular Injury of Nervous System

*432 **Pathology** Team*

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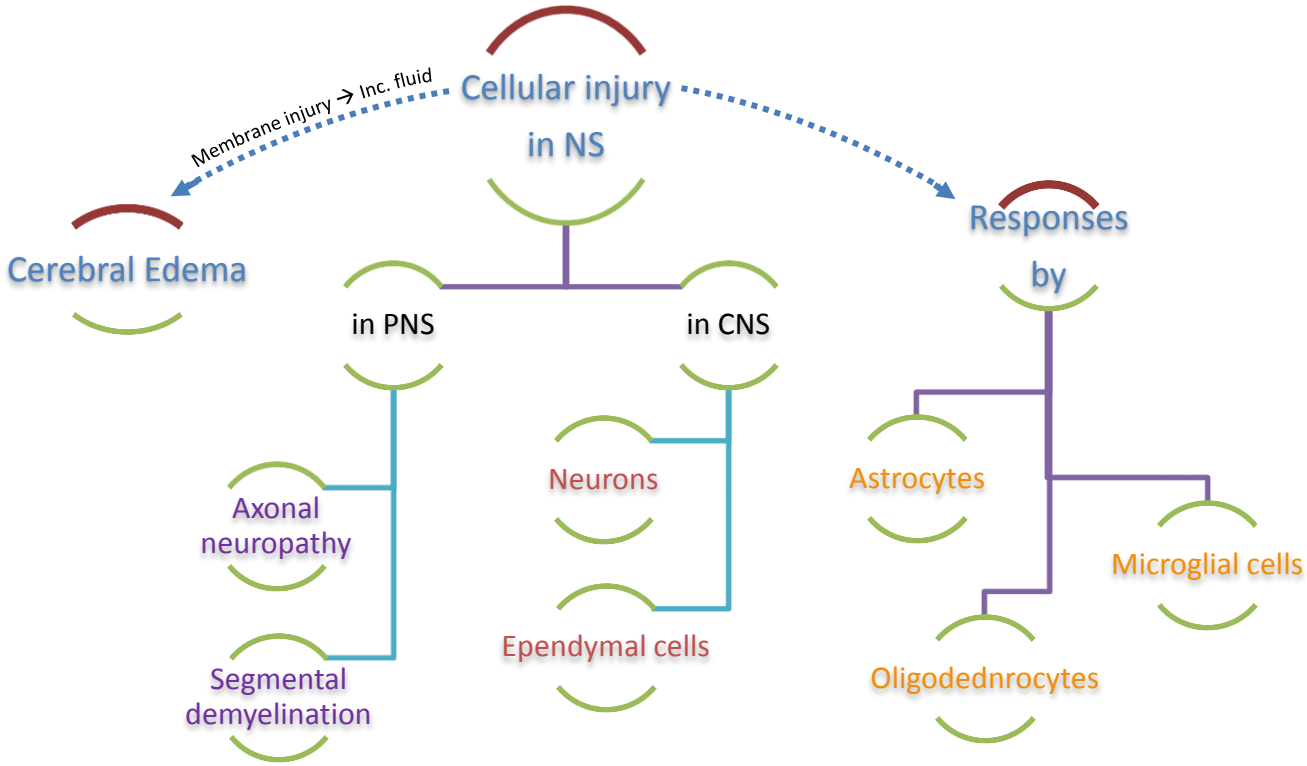
CNS Block

Color Index: female notes are in purple. Male notes are in Blue. Red is important. Orange is explanation.

Cellular injury in nerves system and cerebral edema

Mind Map:

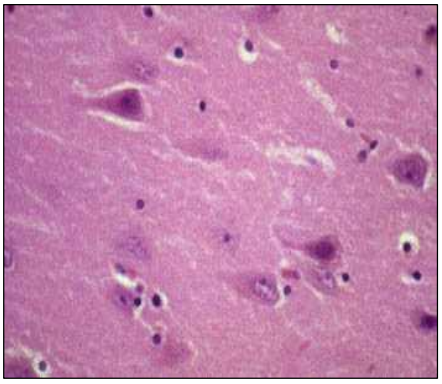


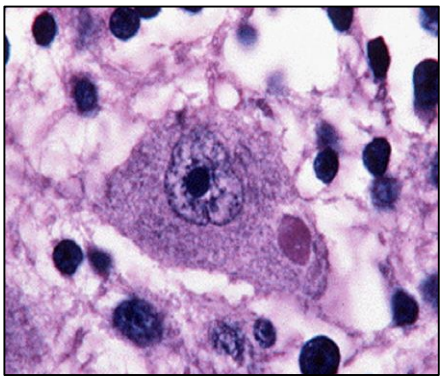
Neuronal Injury

Neuronal Injury in CNS is a number of changes occur in neurons and their processes. Could be detected by H & E (hematoxyline & eosin) 12 hours after having hypoxic-ischemic insult (or any acute injury).

Markers of Neuronal Injury in Cell Bodies:

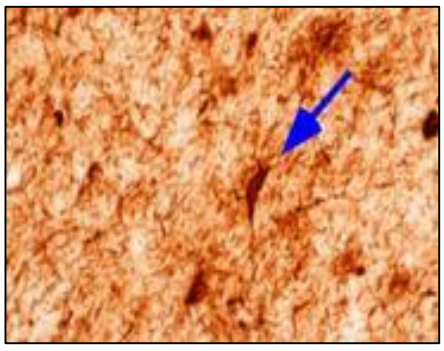
1) **Red Nucleus**
- Shrinkage of the cell body
- Pyknosis of the nucleus (irreversible condensation of chromatin). What we can see in Necrosis as well.
- Disappearance of the nucleolus
- Loss of Nissl substance
- Intense eosinophilia of the cytoplasm *("red neurons")*





2) **Intracellular inclusions** (Typical in infection)
Nuclear or cytoplasmic aggregates of stainable substances, usually proteins. Ex: Negri bodies in rabies

3) **Dystrophic neurites**
In some neurodegenerative diseases, neuronal processes become thickened and tortuous.



NOTE: A neurite refers to any projection from the cell body of a neuron (dendrites or axons)

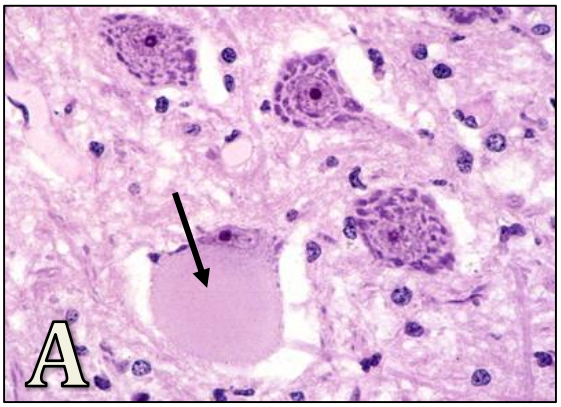
REMEMBER: acute injuries typically result in breakdown of the blood brain barrier and variable degrees of cerebral edema.

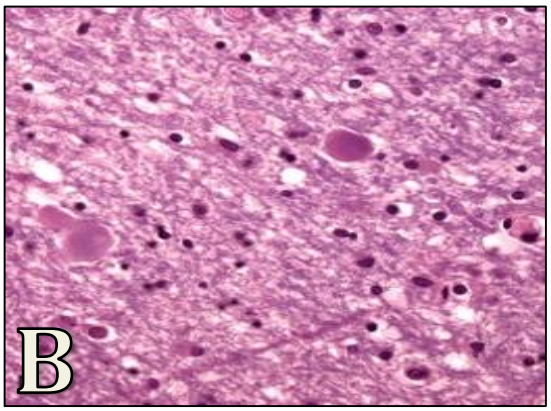
Markers of Neuronal Injury in Axons

- Injured axons undergo swelling (called **spheroids**) and show disruption of axonal transport ***(See picture B)***

- Evidence of injury can be highlighted by **silver staining** or **immunohistochemistry** for axonally transported proteins such as amyloid precursor protein.

- Axonal injury also leads to **cell body enlargement** and rounding, peripheral displacement of the nucleus, enlargement of the nucleolus, and dispersion of Nissl substance (from the center of the cell to the periphery, so-called *central chromatolysis*) ***(See picture A)***





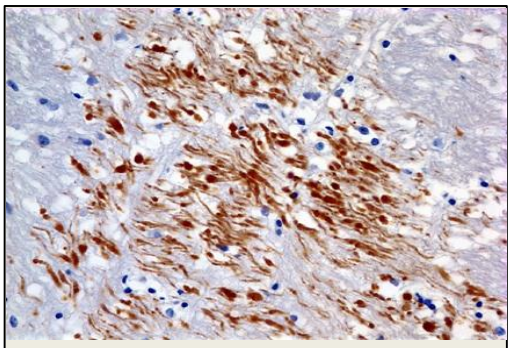
Spheroids: is an injury affecting axons (white matter)
Central Chromatolysis: is an injury affecting cell bodies *(gray matter)(axon injury → protein accumulation in the cell body → enlarged cell body → central chromatolysis)*

Diffuse axonal injury

As many as 50% of patients who develop coma shortly after trauma, even without cerebral contusions (without changing of cerebral color), are believed to have white matter damage and diffuse axonal injury

The movement of one region of brain relative to another (like in accidents) is thought to lead to the disruption of axonal integrity and function.

Can be organized on H & E, or highlighted by silver stain or immunohistochemistry.



Immunostains with antibodies to Beta Amyloid Precursor Protein can detect the axonal lesions in 2-3 hours after the injury

NOTE: Immunostains with antibodies to Beta Amyloid Precursor Protein (BAPP) can detect the axonal lesions in 2-3 hours after the injury (Diffuse axonal injury = spread injury)

Cerebral Edema

Risk Factor

Having accumulation of excess fluid within a fixed area will press on the nerve tissue in CNS. Nerve tissue is so sensitive and exposing to any pressure might damage it. The brain could herniate if it explode to pressure

Types of Cerebral Edema

There are two types, which often occur together particularly after generalized injury:

Vasogenic edema

When blood-brain barrier disrupted, it allows fluid to move freely to the **extracellular** spaces of the brain.

Types:

1. **localized** e.g. inflammation or tumors increased vascular permeability
2. **Generalized**

Cytotoxic edema

An increase in **intracellular** fluid due to neuronal & glial membrane injury, generalized hypoxic-ischemic insult or exposure to some toxic.

Response to Injury

1) Astrocyte

Function

Responsible of repair and scar formation in the brain (**gliosis**) (Note: Fibroblast participate in healing after brain injury to a limited extent except in penetrating brain trauma or around abscesses).

In response to injury, Astrocytes will go into two stages when start repairing:

1- Gemistocytic astrocyte

- Astrocytes undergo hypertrophy & hyperplasia.
- Logically the nucleus enlarges and becomes vascular, and nucleolus is prominent to help in repairing and produce protein to repair.
- The injured tissue astrocyte (characterized by: ramifying processes, cytoplasm takes on a bright pink hue, cell body extends multiple stout).

2- Fibrillary astrocyte (in long-standing gliosis)

- Cytoplasm shrinks in size
- Cellular processes become more tightly interwoven.
- Rosenthal Fibers are seen at this stage.

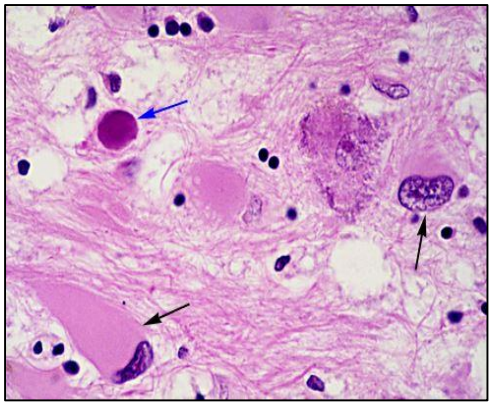
In cerebral abscess in the beginning the astrocyte become larger (called gemistocytic) but if this abscess has been for long time the astrocyte become elongated (called fibrillary).

NOTE: ***Rosenthal fibers*** **are thick, elongated, brightly eosinophilic protein aggregates that can be found in astrocytic processes in chronic gliosis and in some low-grade gliomas.**

REMEMBER:
Gliosis: Reactive change of glial cells in response to damage to the CNS and involves proliferation and hypertrophy.
Glioma: Tumor of glial cells.

2) Oligodendrocytes

- Produce myelin
- In progressive multifocal leukoencephalopathy viral inclusions usually (HIV) can be seen in oligodendrocytes, with a smudgy, homogeneous-appearing enlarged nucleus. (multifocal= multiple location, leuko= white matter, encephalo= brain)



3) Ependymal cells

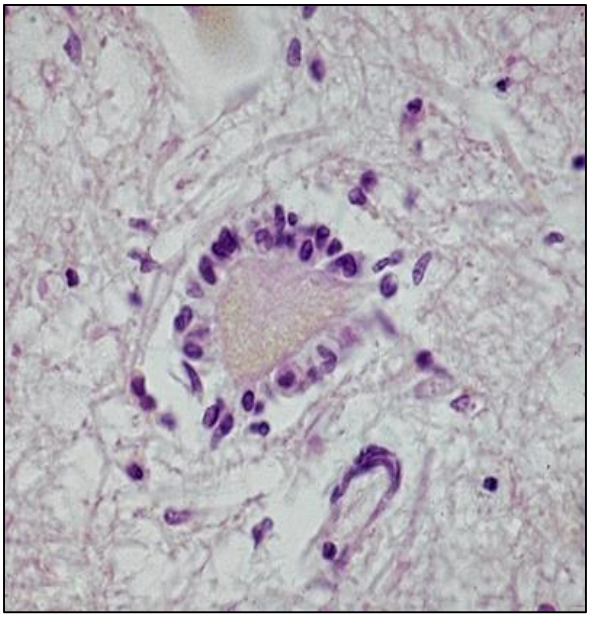
- Lining ventricular system and central canal of the spinal cord.
- **Choroid plexus:** Is in continuity with ependymal. Its specialized epithelial covering is responsible of forming CSF.
- Certain pathogens, particularly cytomegalovirus (CMV), can produce extensive ependymal injury, with typical viral inclusions

4) Microglia

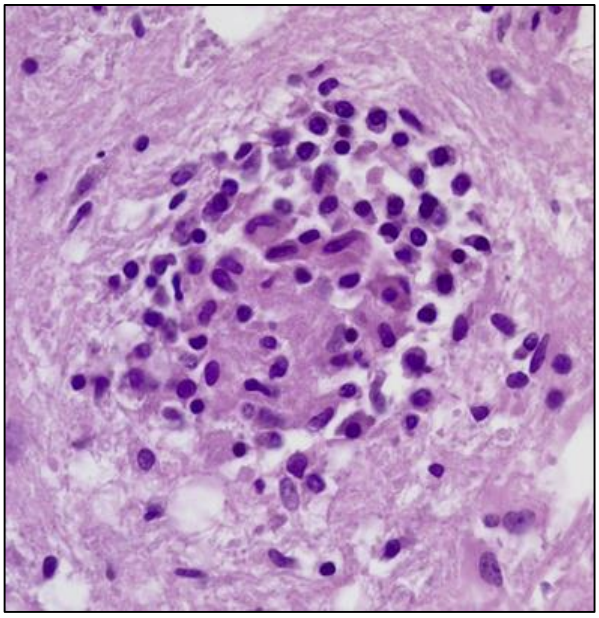
- Bone marrow-derived cells
- Function as the phagocytes of the CNS
- When activated, they proliferate and become more evident
- They may act as **macrophages** after an injury in areas of:
  - Demyelination
  - Organizing infarct
  - Hemorrhage
  - They develop elongated nuclei (*rod cells*) in neurosyphilis or other infections

When these elongated microglia form aggregates at sites of tissue injury, they are termed ***microglial nodules***

Similar collections can be found congregating around portions of dying neurons, termed ***neuronophagia*** (e.g. viral encephalitis).



Neuronophagia



Microglial nodule

Peripheral Nerve injury

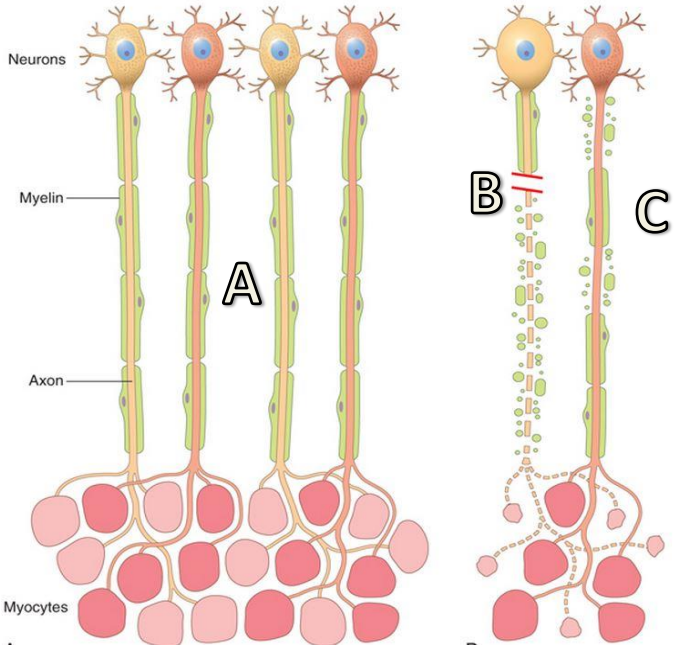
Most of the peripheral neuropathies can be classified as either Segmental demyelinating or axonal injury, even that some diseases have **mixed** features.

Axonal neuropathies

1. Caused by insults that **directly injure axons.**
2. The **entire distal portion** of an affected axon degenerates.
3. Axonal degeneration is associated with secondary myelin loss a process sometimes referred to as **Wallerian** degeneration
4. Regeneration takes place through axonal regrowth and subsequent remyelination of the distal axon.
5. The morphologic hallmark of axonal neuropathies is a decrease in the density of axons, which in electrophysiologic studies correlates with a decrease in the strength of amplitude of nerve impulses.

Segmental demyelination

1. Demyelinating neuropathies are characterized by **damage to Schwann cells or myelin** with **relative axonal sparing**, resulting in ***abnormally slow nerve conduction velocities***
2. Demyelination typically occurs in individual myelin internodes randomly; this process is termed segmental demyelination (segments of axon)
3. Morphologically, demyelinating neuropathies show a relatively **normal density of axons** and features of segmental demyelination and repair → recognized by the presence of axons with **abnormally thin myelin sheaths and short internodes**



A- Normal axons
B- Axonal injury
C- Segmental demyelination

Summary (from Robbins Basic Pathology)

Cerebral edema is the accumulation of excess fluid within the brain parenchyma.
Increase in brain volume (as result increased CSF volume, edema, hemorrhage, or tumor) raise the pressure inside the fixed capacity.

Questions

1/ what is the most common injury to the brain?
Ischemia, virus, degenerative disease, autoimmune disease.

2/ what is the two elements important to the brain cells to work?
Oxygen and glucose

3/ where can we have a diffuse axonal injury?
Accidents

4/ what kind of necrosis we see it in the brain?
Liquefactive necrosis

5/ what component of the cell will loss in case of red nucleus?
Nissl bodies

6/ which disease we can see negri bodies?
Rabies

7/ what is the appearance under the microscope in neurodegenerative disease?
Dystrophic neurites

8/ what is the characteristic features of diffuse axonal injury?
Asymmetric distribution of axonal swellings (spheroids)

اللهم إني استودعك ما قرأت و ما حفظت و ما تعلمت فرده عليَ عند حاجتي إليه انك على كل شيء قدير

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*Good Luck ^_^*