CNS Cellular Aspects of Injury and Pathological Aspects of CNS Trauma

Seham AlArfaj

Mohamed Bohlega

Red: Doctors' and important notes.
Green: Team notes.

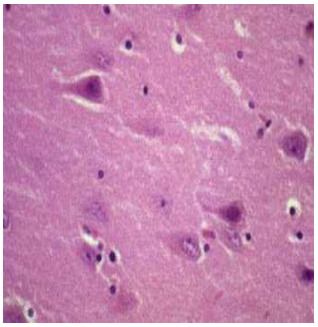
PATTERNS OF CELLULAR INJURY IN THE NERVOUS SYSTEM:

Markers of Neuronal Injury:

Examples:

1. Red neuron:

Cause and description: within 12 hours of an irreversible hypoxic/ischemic insult, *acute neuronal injury* becomes evident even on routine hematoxylin and eosin (H & E) staining:

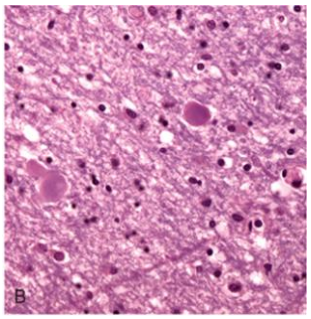


- shrinkage of the cell body
- pyknosis of the nucleus
- disappearance of the nucleolus
- Loss of Nissl substance.

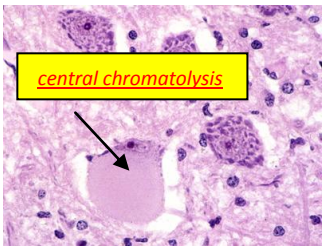
Nissl Substance: is a material consisting of granular endoplasmic reticulum and ribosomes and occurring in nerve cell bodies and dendrites. Also called *Nissl body*, *Nissl granule*

- intense eosinophilia of the cytoplasm *("red neurons")*

2. Axonal injury:



- Injured axons undergo swelling (called spheroids) and show disruption of axonal transport.
- Axonal injury also leads to *central chromatolysis* which is characterized by 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).



Seen by: silver staining or immunohistochemistry for axonally transported proteins

Reminders!

→ ***Describe specific intracellular inclusions in Parkinson's disease and Alzheimer's disease.***

Answer: Alzheimer: **Neurofibrillary tangles, which are mostly composed of hyperphosphorylated tau** Parkinson: lewy bodies

→ ***In which neurodegenerative disease the neruonal processes become thickened and tortuous?***

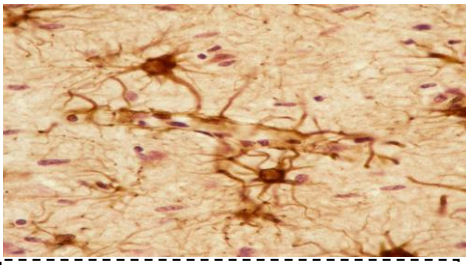
Answer: Alzheimer's disease

→ ***Mention another two examples of cell injury where the cells can exhibit intracellualr inclusions.***

Answer: 1) In old people, complex lipids can cause cellular inclusions called *lipofuscin*.

2) Viral infections of the CNS can cause intracellular inclusions.

Astrocytes in Injury and Repair:

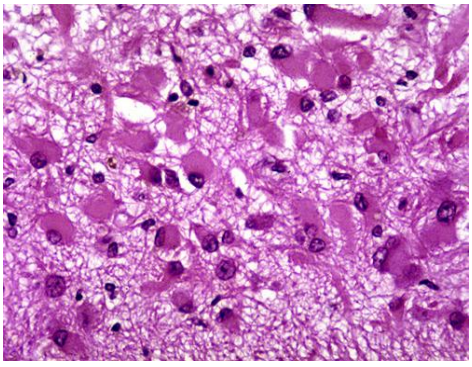


Glial fibrillary acidic protein (GFAP): is a **Staining** Protocol for Immunohistochemistry that is cell-specific marker that generally distinguishes active astrocytes from other glial cells.

Astrocytes are the principal cells responsible for repair and scar formation in the brain, a process termed *gliosis*

In response to injury:

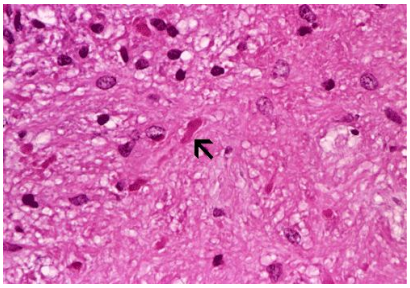
- Astrocytes undergo both hypertrophy and hyperplasia
- The nucleus enlarges and becomes vesicular (pale), and the nucleolus is prominent
- The previously scant cytoplasm expands to →***(gemistocytic astrocyte)*** which is a bright pink, somewhat irregular swath around an eccentric nucleus, from which emerge numerous stout, ramifying processes



Gemistocytic gliosis

- In settings of long-standing gliosis, astrocytes have less distinct cytoplasm and appear more fibrillar ***(fibrillary astrocytes)***
- There is **minimal** extracellular matrix deposition: Unlike the repair after injury elsewhere in the body, fibroblasts participate in healing after brain injury only to a limited extent (usually after penetrating brain trauma or around abscesses)

Rosenthal fibers are intracellular accumulation.



Charcterized by : thick, elongated, brightly eosinophilic protein aggregates that can be found in astrocytic processes in chronic gliosis and in some low-grade gliomas

→ ***Which tumor exhibits Rosenthal fibers?***

Pilocytic astrocytoma

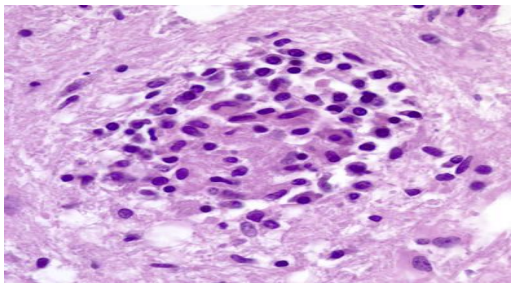
Microglia in Injury and Repair:

Microglia:

- Bone marrow-derived cells
- Function as the phagocytes of the CNS
- When activated, they proliferate and become more evident
- They may be recognizable as activated macrophages in areas of:
    1. Demyelination
    2. Organizing infarct
    3. Hemorrhage
    4. They develop elongated nuclei (*rod cells*) in neurosyphilis or other infections

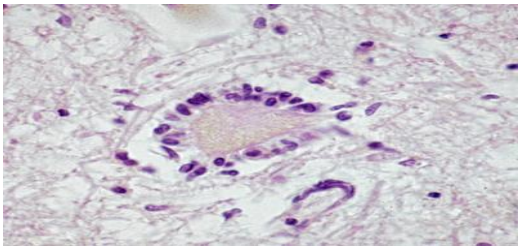
Example of microglial changes in injuries:

- *microglial nodules*: is when elongated microglia form aggregates at sites of tissue injury. e,g in viral infection



Microglial nodule

- *Neuronophagia*: when microglia are found congregating (gathering) around portions of dying neurons



Neuronophagia

CNS trauma

The site has a crucial rule:

Injury of several cubic centimeters of brain parenchyma may be clinically silent (e.g. frontal lobe), severely disabling (e.g. spinal cord), or fatal (e.g. brain stem)

The magnitude and distribution of traumatic brain lesions depend on:

- the shape of the object causing the trauma
- the force of impact
- whether the head is in motion at the time of injury

A blow to the head may be: *penetrating* or *blunt;* it may cause an *open* or a *closed injury*.

In Severe brain damage can occur in the absence of external signs of head injury, and conversely, severe lacerations and even skull fractures do not necessarily indicate damage to the underlying brain

In addition to skull or spinal fractures, trauma can cause parenchymal injury and vascular injury; combinations are common

Examples on CNS trauma:

1. Contusion
2. Laceration
3. Diffuse axonal injury
4. Concussion

Contusion is hemorrhage within the tissue while laceration means cutting

1. Contusion (bruising):

Caused by: - rapid tissue displacement e.g: sudden movement of the brain

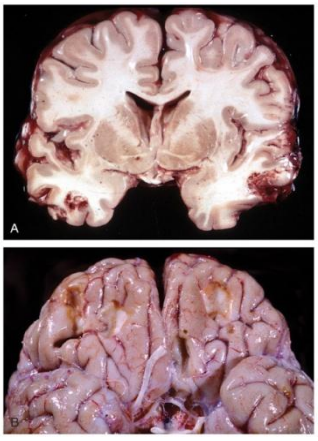
- disruption of vascular channels, and subsequent hemorrhage, tissue injury, and edema

Susceptibility: Since they are the points of impact, crests of gyri are most susceptible, whereas cerebral cortex along the sulci is less vulnerable

Locations: the frontal lobes along the orbital gyri and the temporal lobes are the most common sites because they are the most frequent sites of direct impact and those are the regions of the brain that overlie a rough and irregular inner skull surface.

In alcoholic: it is the occipital lobes

2. Laceration (tear):



Definition: is when there is tissue tearing, vascular disruption, hemorrhage, and injury along a linear path.

Causes: penetration of the brain, either by a projectile such as a bullet or a skull fragments from a fracture.

3. Diffuse axonal injury :

Definition: Widespread injury to axons within the brain can be very devastating

Causes:

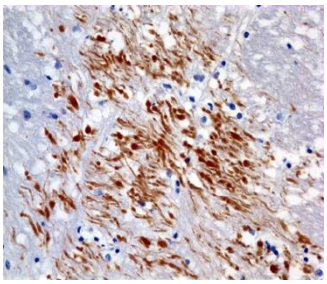
- the movement of one region of brain relative to another is thought to lead to the disruption of axonal integrity and function
- Angular **acceleration** alone, in the absence of impact, may cause axonal injury as well as hemorrhage

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

Location: Although these changes may be widespread, lesions are most commonly found near the angles of the lateral ventricles and in the brain stem.

Characteristics: wide but often asymmetric distribution of axonal swellings that appears within hours of the injury and may persist for much longer

Demonstrated: with silver stains or by immunohistochemistry for proteins within axons



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

+ve is in brown color

4. Concussion:

Description: reversible altered consciousness from head injury in the absence of contusion

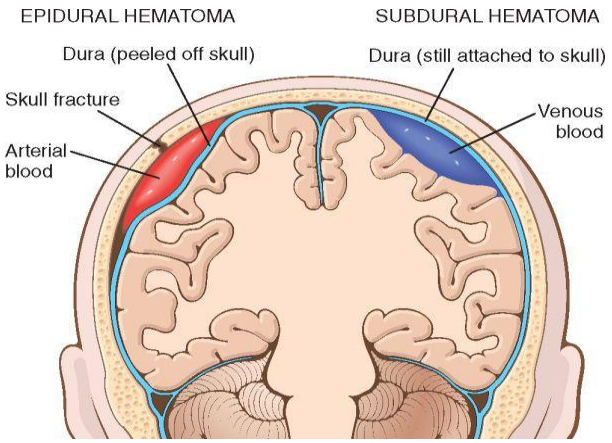
The characteristic transient neurologic dysfunction includes loss of consciousness, temporary respiratory arrest, and loss of reflexes

The pathogenesis of the sudden disruption of nervous activity is unknown

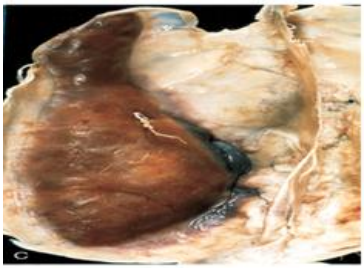
Recovery: neurologic recovery is complete but amnesia for the event persists

Traumatic Vascular Injury:

- Epidural hematoma
- Subdural hematoma



1. Epidural (extradural) Hematoma:



Normally: the dura is tightly applied to the inside of the skull, fused with the periosteum.

The most important vessels in the dura: are the middle meningeal arteries which are vulnerable to injury, particularly with skull fractures.

Mechanism:

- In children, in whom the skull is deformable, a temporary displacement of the skull bones may tear a vessel in the absence of a skull fracture.
- Once a vessel has been torn, the accumulation of blood under arterial pressure can cause separation of the dura from the inner surface of the skull.
- The expanding hematoma has a smooth inner contour that compresses the brain surface.

Clinically: patients can be lucid for several hours between the moment of trauma and the development of neurologic signs.

Treatment: drainage because it is a neurosurgical emergency (rapidly progressing).

2. Subdural hematoma

Cause: the rapid movement of the brain that occurs in trauma can tear the bridging veins that extend from the cerebral hemispheres through the subarachnoid and subdural space to empty into dural sinuses

These vessels are particularly prone to tearing, and their disruption leads to bleeding into the subdural space

- In elderly patients with brain atrophy the bridging veins are stretched out and the brain has additional space for movement, accounting for the higher rate of subdural hematomas in these patients, even after relatively minor head trauma
- Infants are also susceptible to subdural hematomas because their bridging veins are thin-walled

Site: they are most common over the lateral aspects of the cerebral hemispheres and are bilateral in about 10% of cases

Manifestation: occur most often within the first 48 hours after injury

- Neurologic signs are attributable to the pressure exerted on the adjacent brain
- These may be focal, but often the clinical manifestations are non localizing and include headache or confusion
- In time there may be slowly progressive neurologic deterioration, rarely with acute decompensation.

Macroscopic:

- Acute subdural hematoma appears as a collection of freshly clotted blood apposed along the contour of the brain surface, without extension into the depths of sulci
- The underlying brain is flattened, and the subarachnoid space is often clear
- Typically, venous bleeding is self-limited → breakdown and organization of the hematoma take place over time

Changes seen:

About 1 week: Subdural hematomas organize by lysis of the clot.

2 weeks: growth of fibroblasts from the dural surface into the hematoma

1-3 months: early development of hyalinized connective tissue

Organized hematomas are attached to the inner surface of the dura and are not adherent to the underlying arachnoid

The lesion can eventually retract as the granulation tissue matures, until there is only a thin layer of reactive connective tissue ("subdural membranes")

Subdural hematomas commonly rebleed (**chronic subdural hematomas**), presumably from the thin-walled vessels of the granulation tissue, leading to microscopic findings consistent with a variety of ages

The treatment of symptomatic subdural hematomas: is to remove the organized blood and associated organizing tissue.

Homework:

Define Corpora amylacea. Where and when they are deposited in the CNS?

Corpora amylacea in the CNS represent a degenerative change in astrocytes and occur in increasing numbers with advancing age. These are located wherever there are astrocytic end processes, especially in the subpial (space under the pia matter) and perivascular zones.

What is a Coup-Contrecoup injury?

When there is impact of an object with the head, injury may occur from collision of the brain with the skull at the site of impact (a coup injury) or on the opposite side (contrecoup) e.g: in car accidents. Both coup and contrecoup lesions are contusions.