Cellular pathology of CNS and few other topics

We have neurons and glial cells - astrocytes - oligodendrocytes - ependymal cells - microglial cells

Each is composed of a cell body and axon

Ali Al Khader, MD
Faculty of Medicine
Al-Balqa Applied University
Email: ali.alkhader@bau.edu.jo
Lecture outline

- Reactions of neurons to injury
- Reactions of glial cells to injury
- Cerebral edema
- Hydrocephalus
- Brain herniation
- Malformations
Reactions of Neurons to Injury

• **Red neurons:**

... = acutely injured neurons

...12-24 hours after an irreversible acute insult (hypoxia, ischemia...etc.)

...the earliest morphological marker of neuronal cell death

...features: -shrinkage of the cell body
  - pyknosis of the nucleus
  - disappearance of the nucleolus
  - loss of Nissl substance
  - intense eosinophilia of the cytoplasm
Reactions of Neurons to Injury, cont’d

• **Subacute and chronic neuronal injury (“degeneration”):**
  ...certain slowly evolving neurodegenerative diseases
  ...such as amyotrophic lateral sclerosis and Alzheimer disease
  ...the characteristic histologic feature is: cell loss
  ...often selectively involving functionally related groups of neurons
  ... + reactive gliosis...the best indicator in early stage (when loss is not apparent yet)
  ...for many of these diseases, the death of cells is by apoptosis

• **Axonal reaction:**
  ...cell body changes due to axonal regeneration
  ...increased protein synthesis necessary for axonal sprouting
  ...-enlargement
    -rounding up of the cell body
    -peripheral displacement of the nucleus
    -enlargement of the nucleolus
  -dispersion of Nissl substance from the center to the periphery of the cell (central chromatolysis)
Reactions of Neurons to Injury, cont’d

• **Subcellular alterations** (on the level of organelles and cytoskeleton)

...we are mainly talking about **neuronal inclusions**:
  - **aging**: intracytoplasmic lipids (lipofuscin), proteins, or carbohydrates
  - genetic disorders of metabolism (**storage diseases**)
  - **viral infections**:
    - herpes: Cowdry body (intranuclear)
    - rabies: Negri body (intracytoplasmic)
    - CMV: (nuclear and cytoplasmic)
  - **neurodegenerative diseases**:
    - intracytoplasmic inclusions in Alzheimer (neurofibrillary tangles)
    - intracytoplasmic inclusions in Parkinson (Lewy bodies)
Reactions of glial cells to Injury...astrocytes

• Gliosis: hypertrophy and hyperplasia of astrocytes...due to any CNS injury
  ...sometimes the astrocytes are markedly enlarged with eosinophilic cytoplasm & eccentric nucleus... = gemistocytic astrocytes

• Alzheimer type II astrocyte...hyperammonemia

• Rosenthal fibers: thick elongated pink intracytoplasmic inclusions in astrocytes
  ...composed of certain heat shock proteins and ubiquitin
  ...in long-standing gliosis, pilocytic astrocytoma, Alexander disease...etc.

• Corpora amylacea (polyglucosan bodies)
  ...faintly basophilic PAS-positive rounded concentrically lamellated structures in astrocytic end processes...composed of GAG polymers, heat shock proteins and ubiquitin
Reactions of glial cells to Injury...microglial cells

• Rod cells: microglial cells with elongated nuclei...neurosyphilis

• Microglial cells are activated in areas of demyelination, infarction, hemorrhage..etc.

Reactions of glial cells to Injury...oligodendrocytes

• Progressive multifocal leukoencephalopathy (PML)
  ...caused by JC papova virus
  ...nuclear inclusions in oligodendrocytes
Cerebral edema

• 2 types:
  - Cytotoxic edema
    ...hypoxia, ischemia or toxins
    ...intracellular
  - Vasogenic edema
    ...disruption of blood-brain barrier
    ...extracellular accumulation
    ...localized (abscess, tumor...etc.)
    or generalized (late in global brain ischemia)

- The brain is soft
- Ventricular cavities are compressed
**Hydrocephalus** = increase in CSF volume within the ventricular system

**Communicating**

**Non-communicating**

Aqueductal stenosis is the most common cause of congenital non-communicating hydrocephalus

Triad in adults:
- ataxia
- dementia
- urinary incontinence

If happened before closure of sutures

**Sunset eyes?**


**Hydrocephalus ex vacuo?**

A mechanical model of ventricular system

**Check https://www.hydroassoc.org/hydrocephalus-awareness-baby-klaus/ for references**
Brain herniation...3 main types

*Compression of ipsilateral 3rd cranial nerve
…ipsilateral pupillary dilation and impaired ocular movements ("blown pupil")
*Posterior cerebral artery compression…1st visual cortex is affected
*With further displacement, compression on contralateral cerebral peduncle (Kernohan’s notch)...ipsilateral hemiparesis (false localizing sign)
*Duret hemorrhages in midbrain and pons (linear or flame-shaped due to tearing of penetrating vessels)...a bad sign

The medial aspect of temporal lobe is compressed

The most dangerous
...often fatal...due to respiratory and cardiac centers compromise
Malformations

• Neural tube defects

...the most frequent type of CNS malformation

...folate deficiency during the first trimester

...maternal screening for elevated α-fetoprotein for early detection...also imaging

...types:

...Spina bifida occulta (asymptomatic bone defect) or spina bifida (with spinal cord deformity and meningeal outpouching)

...Myelomeningocele (most common site: lumbosacral)

...motor, sensory, bladder and bowel problems

...infection through the thin or ulcerated overlying skin

...Anencephaly: absence of forebrain and top of skull

...Encephalocele: mostly posterior. If anterior, may extend to sinuses

Fig. 23.14 Myelomeningocele. Both meninges and spinal cord parenchyma are included in the cystlike structure visible just above the buttocks.
Malformations

- **Forebrain malformations**
  - Microencephaly
    ...small brain volume
    ...usually associated with small head (microcephaly)
    ...associated with:
      - chromosomal abnormalities
      - fetal alcohol syndrome
      - HIV
      - Zika virus
  - Megalencephaly (large head and brain volume)
    ...rare genetic disorders
  - Holoprosencephaly (midline problems)
    ...some forms are associated with cyclopia
Malformations

• Posterior fossa anomalies

-Arnold-Chiari malformation...Chiari type I and Chiari type II malformations

-Dandy-Walker malformation (enlarged posterior fossa, absence of the cerebellar vermis, and a large midline cyst)
Thank You