Pathology Revision of CNS Block (Midterm)

@Pathology434

Done By:

Hussain Al-Kaff & Omar A Rahbeeni

***For Any correction contact me:**
pathology434@gmail.com
*** if you have any quistion, Ask us here: http://Ask.fm/pathology434**

1-Cellular Injury of Nervous System:

Markers of Neuronal Injury.

1-Red neuron:

early irreversible hypoxic/ ischemic insult, acute neuronal injury (within 12 hours) and becomes leads to:
– shrinkage of the cell body, pyknosis of the nucleus, disappearance of the nucleolus, loss of Nissl substance and intense eosinophilia of the cytoplasm.

2-intracellular inclusions:

stainable substances(protein) aggregates in Nuclei or cytoplasm.

3-dystrophic neurites:

-axons become thickened and tortuous, in Neurodegenerative diseases: Ex: (Parkinson,Alzheimer).

4-Axonal injury:

characterized by:

- **swelling of axons and disrupted of axonal transport (called spheroids).**
- **Enlargement of cell body, enlargement of nucleolus and dispersion of Nissl substance (central chromatolysis).**

Diffuse Axonal injury:

after traumas, it is asymmetrical distribution in wide area and there is a loss of axonal function.
can be showed by silver staining or immunohistochemistry with antibody to (Beta Amyloid Precursor Protein) (BAPP): can detect the axonal lesions in 2-3 hours after the injury.

Markers of peripheral nerve injury.

Axonal neuropathies:

-axon degenerates (decrease in the density of axons > decrease in strength of impulse).
-secondary myelin loss (Wallerian degeneration).

Segmental demyelination (Demyelinating neuropathies):

-damage to Schwann cells or myelin > decrease in impulse velocity (normal density of axons).

Injury of Astrocytes.

-Astrocytes undergo both hypertrophy and hyperplasia.
1-Gemistocytic Astrocytes: Enlargement nucleus, prominent nucleolus, cytoplasm expands and take bright pink color, cell extends stout and ramifying processes.

2-fibrillary astrocytes: astrocytes have less distinct cytoplasm and appear more fibrillar (usually in long-standing gliosis)

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

Injury of Oligodendrocyte.

in progressive multifocal leukoencephalopathy and viral inclusions become *smudgy homogeneous-appearing enlarged nucleus .*
-injuries of oligodendrocytes occur in white matter.

Injury of ependymal cell.

in cytomegalovirus (CMV).

Injury of Microglia.

They become elongated nuclei (rod cells) in neurosyphilis or other infection.
-microglial nodules: elongated microglia aggregates at sites of tissue injury.
-Neuronophagia: elongated microglia aggregates at sites of dying tissue, (e.g. viral encephalitis).

Cerebral Edema.

1-Vasogenic edema:

blood-brain barrier is disrupted > extracellular edema. due inflammation or tumor.

2-Cytotoxic edema:

An increase in intracellular fluid secondary to hypoxia/ ischemia or some toxin.

2,3-Brain Tumors:

Child: Posterior fossa (20%), Adults: Supratentorial (80%).

General Symptoms:

-Seizures, Vague and Headache.

Classification:

-Cells inside CNS: Glioma, medulloblastoma.
-Cells covering CNS: Meningioma.
-Others: Schwannoma.

1-Gliomas.

3 Tumors: Astrocytoma, Oligodendroglioma, Ependymoma.

A.Astrocytoma:

-Mutations that alter the enzymatic activity of two isoforms of the metabolic enzyme isocitrate dehydrogenase (IDH1 and IDH2) are common in lower-grade astrocytomas.

-Astrocytoma classified into 2 types:

Pilocytic Astrocytoma: Grade 1	**Fibrillary: 3 subtypes:** 1-Diffuse Astrocytoma: Grade 2. 2- Anaplastic Astrocytoma: Grade 3. 3-Glioblastoma Multiforme: Grade 4.

***We will take two types: Pilocytic Astrocytoma (Grade 1) and Glioblastoma Multiforme (Grade 4).**

*Pilocytic Astrocytoma:

-Most common CNS Tumor In Children.
-Benign and well circumscribed.
-Cystic Lesion with mural Nodule.
-Rosenthal Fibers.
-Absence of Mitosis and Necrosis.
-GFAP Positive.

*Glioblastoma Multiforme:

-Most common CNS Malignant Tumor in Adults.
-Cross "Corpus callosum" (Butterfly Pattern).
-Pseudopalisading necrosis.
-Endothelial Proliferation.
-GFAP Positive.
-Primary GB: Associated with EGFR.
-Secondary GB: Associated with P53.

B.Oligodendroglioma:

-in Adults (Supratentorial) and Malignant.
-Loss of Heterozygosity of chromosomes: 1P and 19Q.
-Round Nuclei inside halo cytoplasm (Fried-Egg Pattern).
-interlacing pattern of blood vessels.

C.Ependymoma:

-In Children and Malignant.
-Perivascular Pseudorosettes (No canal).
-Sometimes accompanied with Hydrocephalus.
-Mitosis, Necrosis and less differentiated in Histology.

2-Meningioma.

-Benign Tumor in Adults (Women mostly).
-Mass arising from Arachnoid Cells (Well demarcated) and the mass appear in dura.
-Whorled Pattern.
-Psammoma Bodies.
-Subtypes: 1-Syncytial (without cell membrane), 2-Fibroblastic (with collagen) and 3-Transitional (Combination of two previous types).

-Atypical Meningioma: Grade 2, -Anaplastic (Malignant) Meningioma: Grade 3.

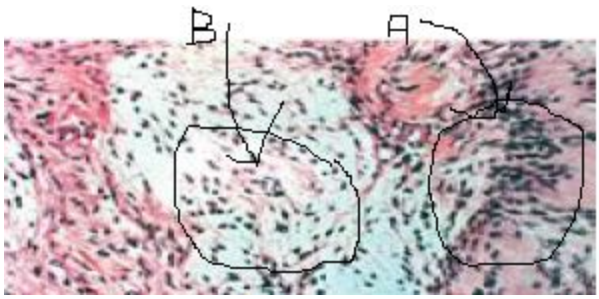
3-Medulloblastoma.

-Highly Malignant tumor in Child (Grade 4) from Granular Cells of Cerebellum.
-Destruction of Superior midline of Cerebellum.
-Small round blue cells and hyperchromatism and Homer wright Rosettes in Histology.

4-Schwannoma.

-Benign tumor in adults from schwann cells.
-Affects Mostly 8th Cranial Nerve.
-Bilateral Acoustic Schwannoma associated with Neurofibroma 2 (NF2).

-Antoni A: More cellular - fibrillary-elongated tissue.
-Antoni B: Less Cellular - loose tissue.
- Nuclear free-zone: Verocay Bodies between the two nuclear palisading.



5-NeuroFibroma.

1-Cutaneous (diffuse) neurofibroma or in solitary neurofibroma: These arise sporadically or multiple lesion in association with NF1, Benign.
2-plexiform neurofibroma: arising in individuals with NF1, malignant.

6-Metastatic tumours.

-Common Places: Lung and breast (most common), skin (melanoma), kidney, and gastrointestinal tract.

-Gross appearance:

- **multiple , well circumscribed.**
- **Sharply demarcated lesion at gray matter with edema.**

4-Multiple Sclerosis:

-Autoimmune disease in young adults (Women mostly), Affects myelin sheath of cranial nerves and Oligodendrocytes.

*Risk Factors:

1- 15 fold higher in first degree relatives.
2- Monozygotic twins more than dizygotic twins.
3- Genetic risk: Mutation in HLA-DR2 gene

*Pathogenesis:

-Combination of environmental (such as infection) & genetic factors that result in a loss of tolerance of self proteins (antigen) → Antigen presenting Cell comes and activates T-helper (CD4) → secret cytokines IL2 and IL7 → T cell cross BBB → Type IV hypersensitivity → infiltrate of lymphocytes, macrophages,B Cells and plasma cells produce antibody → demyelination, axonal loss and sometimes even leading to neuronal death.

*Gross Features:

-Grey-tan irregular lesion in white matter (Plaques).
-Plaques found usually in Ventricles, optic nerve, Brain stem, cerebellum and spinal cord.

Active Plaques	Inactive Plaques
increase Macrophages	Decrease Oligodendrocytes
Myelin debris	No Myelin
Present of monocytes and lymphocytes	No inflammation
-	increase astrocytes (For gliosis)

*Symptoms:

-Visual impairment (Blurred vision).
-Ataxia.
-Weakness of Muscles and Fatigue.
-Sexual Dysfunction.
-Vertigo and Spanning speech.
-Loss of sensation of lower limb.

*CSF Finding:

1-increase in γ-globulin.
2-Increase in others proteins generally.
3-Pleocytosis (WBC Increased).
4-Oligoclonal Bands.

*Management:

-Interferon-Beta with Steroids.

Good Luck