وقل رب زدني علماً

النادي الطبي

PERIPHERAL NERVOUS SYSTEM

SUBJECT : Pathology - TABLES

LEC NO. : 6

DONE BY : Sami Alodeh

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PNS

Pathology Lecture 6

CNS Infections

PARENCHYMAL INFECTIONS

- Infectious pathogens (viruses, parasites, bacterial)
- In general, viral infections are diffuse, and bacterial infections (when not associated with meningitis) are localized
- While other organisms may produce mixed patterns
- Immunosuppressed hosts show more widespread involvement with any agent

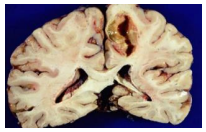
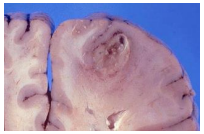
BRAIN ABSCESS

GENERAL FEATURES

- Brain abscesses are most often caused by bacterial infections
- Direct implantation of organisms, or local extension from adjacent foci (paranasal sinusitis, mastoiditis)
- Hematogenous route from heart, lungs or after tooth extraction
- CSF have little role in the diagnosis. Organisms are more reliably cultured by draining the abscess directly
- CLINICAL PRESENTATION: Progressive focal deficit, and signs of increase ICP

GROSSLY

- Discrete lesion with central liquefactive necrosis
- Localized liquefactive necrosis surrounded by granulation tissue & severe edema leading to increase ICP

COMPLICATIONS

- If rupture → ventriculitis, meningitis, and venous sinus thrombosis
- Treatment: Surgery and antibiotics

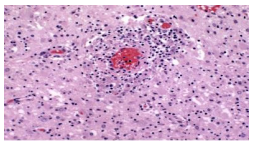
VIRAL ENCEPHALITIS

General Features

Viral encephalitis is a parenchymal infection of the brain that is almost associated with meningeal inflammation (meningoencephalitis)

FEATURES common to most viral infections:
- Perivascular and parenchymal mononuclear cell infiltrates
- Microglial nodules & neuronophagia
- Characteristic inclusion bodies

**Prominent perivascular inflammatory cell infiltrates indicative of viral encephalitis



Examples

- ARBO VIRUSES (West Nile, Equines,… etc)
- HSV1 & HSV2
- Herpes Zoster
- CMV
- POLIO
- RABIES
- HIV
- JC (Progressive Multifocal Leukoencephalopathy)
- Measles (Subacute Sclerosing Panencephalitis)

1. Viral Encephalitis

1) Herpes Simplex Virus Type 1&2

HSV1 (>90% of cases)

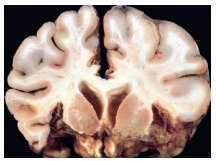
- Children or young adults
- Hemorrhagic necrotizing inflammation in temporal lobe & orbital gyri of frontal lobe
- SYMPTOMS: alteration in mood, memory, and behavior
- MORPHOLOGY: all common features of viral encephalitis seen + (Cowdry type A) intranuclear viral inclusions in neurons & glial cells

HSV2 (less common)

- In adults may cause meningitis
- Disseminated severe encephalitis occurs in many neonates born by vaginal delivery to women with active primary HSV genital infections

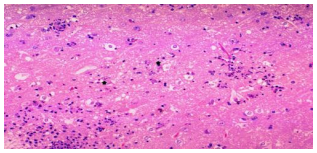
Gross & Morphological Features

Herpes encephalitis showing extensive destruction of inferior frontal and anterior temporal lobes.



Herpes encephalitis
Basal view of the hemorrhagic lesion in the right medial temporal lobe.

Herpes encephalitis
Numerous intranuclear Cowdry A inclusions



2) Varicella-Zoster Virus (Herpes-Zoster)

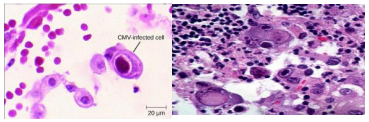
General Features

- Causing Chicken pox during primary infection in children.
- Latent infection in dorsal root ganglia
- Reactivation in adults (Shingles): painful vesicular skin eruption along a dorsal nerve in one or a few dermatomes, Self-limited
- In immunosuppressed patients, may show acute encephalitis

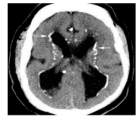
3) Cytomegalovirus CMV

General Features

- Immunosuppressed especially AIDS:
subacute encephalitis in any region & any cell but mainly Paraventricular subependymal region of the brain → Severe hemorrhagic necrotizing ventriculoencephalitis



- Fetus: (CMV IS PASSED TO FETUS THROUGH PLACENTA)
intrauterine infection causes periventricular necrosis and brain destruction, followed later by microcephaly with periventricular calcification

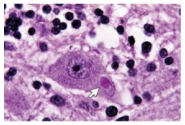

periventricular calcification

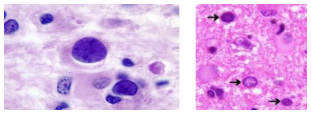
4) Rabies Virus

General Features & Symptoms

- Severe encephalitis (fatal)
- Transmitted to humans by bite of a rabid animal such as dog
- Ascends along peripheral nerve from bite site
- SYMPTOMS:
headache, fever, extraordinary CNS excitability, periods of mania and stupor
- Neuronal degeneration and inflammatory reaction, most severe in brain stem

NEGRI BODIES:
cytoplasmic, eosinophilic inclusions in pyramidal neurons of the hippocampus & Purkinje cells of cerebellum,
in sites usually devoid of inflammation


Negri bodies

5) Poliovirus	**General Features**	- Enterovirus causing mild gastroenteritis - Involvement of CNS in the non-immunized ACUTE: mononuclear cell perivascular cuffs and neuronophagia of the anterior horn motor neurons of the spinal cord CHRONIC: loss of neurons and atrophy of the anterior (motor) spinal roots, and neurogenic atrophy of muscle.	
	Clinical Presentation	- Flaccid paralysis with muscle wasting - Death can occur from paralysis of the respiratory muscles in acute phase	
6) HIV	**General Features**	- Early: aseptic viral meningitis in 10% - Chronic: HIV Encephalitis >> chronic inflammatory reaction with widely distributed microglial nodules with multinucleated giant cells - HIV can directly cause meningoencephalitis, or indirectly affect the brain by increasing the risk for opportunistic infections (toxoplasmosis, CMV) or CNS lymphoma -HIV- associated dementia	
7) JC VIRUS → PML	**General Features**	- Caused by JC polyomavirus exposure during childhood - Reactivation mainly in AIDS patients & other immunosuppressed patients - Infect oligodendrocytes - RESULT: Progressive demyelination of white matter	
	Morphology	**Grossly**	- Patches of irregular, ill-defined destruction of white matter from mm to extensive involvement of the entire lobe
		Microscopy	- Patches of demyelination, with scattered lipid laden macrophages at the center, and reduced number of axons Enlarged oligodendrocyte nuclei with viral inclusions At the edges of the lesion are greatly enlarged oligodendrocyte nuclei whose chromatin is replaced by glassy appearing amphophilic JC viral inclusions 

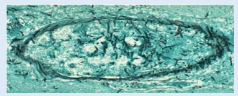
2. Fungal Encephalitis & Other Meningoencephalitides

FUNGAL ENCEPHALITIS

- Candida, Cryptococcus, Aspergillus, & Mucormycosis
- Mainly in immunocompromised patients
- Hematogenous or direct invasion
- Parenchymal granulomas or abscesses, often associated with meningitis
- AIDS patients are prone to cryptococcal meningoencephalitis

Aspergillus fumigatus

Tends to cause a distinctive pattern of widespread septic hemorrhagic infarctions because of its marked predilection for blood vessel wall invasion with subsequent thrombosis

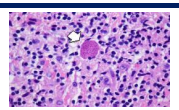


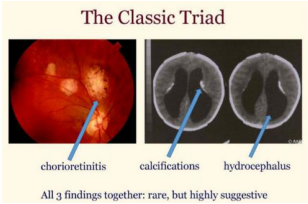
GMS Stain

Toxoplasmosis

Cerebral Toxoplasmosis:

- Immuno-compromised patients, especially (AIDS)
- Small, usually multiple abscesses & necrotic foci
- Both free tachyzoites and encysted bradyzoites may be found at the periphery of the necrotic foci
- IN NEWBORNS (CONGENITAL TOXOPLASMOSIS) who are infected in utero: triad of chorioretinitis, hydrocephalus, and intracranial calcifications





Prion Diseases

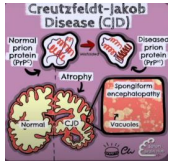
- A group of infectious diseases in which the causative agent is an abnormal form of a cellular protein
- The causative protein > prion protein (PrP), may undergo a conformational change from its normal shape (PrPc) to an abnormal conformation called PrPsc

Include a variety of conditions:
- Sporadic and familial Creutzfeldt- Jacob Disease (CJD)
- Scrapie in sheep
- Bovine spongiform encephalopathy in cattle ("mad cow disease")

Creutzfeldt-Jacob Disease (CJD)

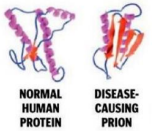
Epidemiology & General Features

- 1 per million incidence, 7th decade
- Sporadic cases 85%
- Familial cases (15%), younger
- Rapidly progressive dementia
- Onset of subtle changes in memory and behavior to death is only 7 months
- FATAL, no treatment known, like ALL prion diseases



Cause & Consequences

- CJD is caused by abnormal proteins called prions that are not killed by standard methods for sterilizing surgical equipment
- As prions build up in cells, the brain slowly shrinks, and the tissue fills with holes until it resembles a sponge
- Those affected lose the ability to think and to move properly and suffer from memory loss
- It is always fatal, usually within one year of onset of illness



Microscopy

- Multifocal spongiform transformation (Intracellular vacuoles in neurons and glia) of cerebral cortex & deep gray matter.
- No inflammatory infiltrate is present.
- ADVANCED CASES: neuronal loss and gliosis