CNS Infections

DEFINITION

1. meningitis
2. Lymphocytic pleocytosis – increased WBCs in the CSF
3. Meningeal carcinomatosis
4. Aseptic meningitis – nonbacterial Meningitis, or inflammation of the subarachnoid space, generally viral; usually self-limited and results in a **lymphocytic pleocytosis**
5. Cerebritis – purulent parenchymal infection of the brain
6. Cerebral abscess – walled-off collection of pus; organized cerebritis
7. Subdural empyema – collection of pus in between the arachnoid and the dura
8. Encephalitis – NON-PURULENT parenchymal infection of the brain; usu. viral;

Pathological Features of Encephalitis

- perivascular mononuclear cell cuffing (chronic inflammatory cells)
- **** **microglial nodules** (hallmark)
- parenchymal chronic inflammation
- parenchymal necrosis
- neuronophagia
- +/- viral inclusions

Route of Entry of Organisms

- hematogenous is the most common
- direct spread – sinuses, oral cavity, or abscess
- trauma or iatrogenic implantation
- peripheral nervous system – retrograde ascension (Ex. HSV, and Rabies)

MENINGITIS

Acute Pyogenic Menigitis

Most causative organism according to age:		
Neonate	E. Coli and Group B Strept	
Infants	H. Influenza	Basilar exudate
Teens/ young adults	N. meningitidis	Cortex
Elderly	Pneumococcus	Cortex

- Clinical Presentation
  - CSF: ⇑ Neutrophils, ⇑ Protein, ⇓ Glucose
  - MRI: enhanced meningeal enhancement
  - Symptoms: headache, neck stiffness, altered mental status
  - MUST CULTURE AND GRAM STAIN
- Morphology
  - GROSS
    - cloudy leptomeninges with engorged, congested vasculature
    - subarachnoid exudate
  - MICRO
    - Neutrophils fill and expand a severely congested subarachnoid space

- Sequelae
  - leptomeningeal fibrosis & resultant communicating hydrocephalus 2^{o} to scarring of the absorptive arachnoid villi
  - Particularly prominent in pneumococcal – excess production of capsular polysaccharides promotes chronic adhesive arachnoiditis

Aseptic (viral) Meningitis

- Clinically, less fulminant than bacterial meningitis
- Organisms: echovirus, nonparalytic poliovirus, and coxsackievirus
- CSF: lymphocytic pleocytosis, normal glucose, +/- inc. protein

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ABSCESS

- usually form hematogenous spread
- Patients present with: fever, focal deficit, and increased ICP signs and symptoms

CSF

- ⇑ protein (may or may not show)
- ⇑ WBCs (polys and monos)
- Normal glucose

Complications

- rupture into ventricles
- dural extension with Superior Sagittal sinus thrombosis
- meningitis
- herniation w/ increased ICP

Pathology of Abscess

from middle to outer

- central collection of pus ⇒ granulation tissue rim w/ chronic inflammation⇒ reactive gliosis ⇒ surrounding vasogenic edema

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EMPYEMA

- usually from infection of the sinuses or skull with contiguous spread to the subdural space

Complication

- worst: S.Sagittal Sinus thrombosis 2^{o} to infection of the vascular channel
- epidural abscess in the spinal cord

Causative agent

- usually S. Aureus

CHRONIC MENINGIOENCEPHALITIS

Tuberculosis

- Clinical presentation: similar to meningitis
  - tends to involve base of the brain: Basilar
  - many time manifests as cranial nerve deficits
  - mild to moderate CSF pleocytosis
  - increased Protein
  - Glucose normal
- Complications
  - obliterative endarteritis w/ cerebral infarction
  - fibrosing arachnoiditis and hydrocephalus
- GROSS
  - basal meningitis
  - gelatinous subarachnoid exudate
  - tuberculoma

- MICRO
  - granulomatous inflammation
  - obliterative endarteritis – mural inflammation and thickened intima

Neurosyphilis
- tertiary syphilis is rare; seen in only 6.5% of untreated cases
- Four Forms:

1. Meningeal Form (Meningovascular)
- chronic meningitis with obliterative endarteritis
- perivascular inflation rich in plasma cells

2. Paretic neurosyphilis
- **ARGYLL-ROBERTSON PUPILS** (accommodate, but don't restrict)
- cerebral atrophy, neuronal loss, microglial nodules, and gliosis
- progressive mental deterioration and severe mood alterations

3. Tabes dorsalis
- involvement of the dorsal roots and ganglia with 2^{o} degeneration of posterior columns
- loss of proprioception, resulting in Charcot's joints, loss of pain sensation and ataxia

4. Gummatous neurosyphilis
- very rare
- parenchymal gummas

VIRAL ENCEPHALITIS

St. Louis Encephalitis
- endemic in S.W. U.S. including Houston
- most prevalent form in U.S.
- Culex "dirty water" mosquitoes are the vector
- June to September most common
- Mortality – 2-12%

Herpes Simplex (Type I)
- most common in children and young adults
- involvement of inferior and medial temproal lobes and orbital gyri
- lethargy, mood change, fever, seixures, behavior change
- **Cowdry A inclusions** common in neurons and glia

Cowdry A Inclusions are seen in:				
HSV	Varicella Zoster	CMV	Progressive multifocal encephalitis	SSPE

- CSF: lymphocytic pleocytosis and hemorrhage
- Neonatal herpes encephalitis may occur in 50% of babies born to women with 1^{o}, active HSV-2 genital infection

Cytomegalovirus (CMV)
- fetus and immunocompromised patients
- In utero: periventricular necrosis, calcification, and microcephaly (All TORCHES give calcification)
- Immunosuppressed: prominent involvement of ependyma & subependymal glia; affects CNS in 15-20% of HIV+ patients

Poliomyelitis
- attacks ventral horns, with loss of neurons and prominent neuronophagia
- End result: flaccidity, hyporeflexia, and muscular atrophy
- Post-polio syndrome
  - occurs approx. 30 years after 1^{o} infection
  - pprogressive weakness in previously unaffected limbs
  - uncertain etiology

Rabies

- retrograde ascension to base of brain and limbic system
- parasthesia around wound w/ headache, fever, and constitutional symptoms is highly suggestive of rabies
- advanced disease: CNS excitability, pharyngeal spasms, mania, coma, death
- **Neuronal eosinophilic cytoplasmic inclusions: Negri bodies.**
- Incubation period: 1 – 3 months (some patients don't remember the bites)
- Rabies is the only viral infection in CNS with ONLY Cytoplasmic inclusions (Negri bodies)

1^{o} HIV Meningoencephalitis

- AIDS dementia
- associated w/ memory loss, apathy, confusion
- MICRO
  - microglial nodules and reactive gliosis
- Vascular myelopathy of HIV
  - nearly identical to chages of Vit B_{12} deficiency
- Childhood CNS disease
  - developmental delay, retardation, and microcephaly
  - calcification of the basal ganglia and white matter

Progressive Multifocal Leukoencephalopathy

- etiological agent: JC virus (a papovirus)
- affects immunosuppressed individuals
- infects oligodendrocytes: results in demyelination and influx of lipid-laden macs
- oligodendrocyte nuclei are enlarges and glassy
- reactive gliosis is exuberant, with bizarre astrocytes

FUNGAL INFECTIONS

- usually basilar
- frequent accompaniment to HIV
- Granulomas seen in only long standing disease and not in HIV
- CSF Cryptococcal antigen assay positive in 98%; India Ink preparations
- *Three Patterns:*
  1. Vasculitis
     - Mucor and Aspergillus
     - Mucor – diabetics with acidosis
  2. Parenchymal invasion
     - Candidia and Cryptococcus
  3. Chronic meningitis
     - Prototype – Cryptococcus

TOXOPLASMOSIS

- highly associated with HIV
- multiple ring-enhancing lesions seen by CT or MRI, with calcification
- Abscesses at gray-white interface
- organisms are seen as free tachyzoites or cysts (bradyzoites)
- in utero – multifocal necrotizing foci with calcification

CYSTERCERCOSIS

- uncooked pork that contains the cysticercus organism
- forms multiple cysts in the brain that become calcified; tend to form at the gray-white interface
- diagnosis: elevated CSF anti-cystercus titer or on clinical findings

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AMOEBIASIS

- rare and fatal
- organism looks like macrophages
- Naegleria fowleri – nasal contraction from infested lakes
- Acanthamoeba – blood borne
- Leptomyxid amoebae – soil-borne – immunocompromised

SPONGIFORM ENCEPHALITIS

- transmitted by Prions (proteins)
- rapidly progressive dementia (3-6 months) with prolonged incubation period (2-35 years)
- no immune response
- incidence increasing
- only iatrogenic implantation is direct implantation of infected tissues
- Pathological features:
  1. Gross
     - may show nothing
     - atrophy with advanced disease
  2. Micro
     - Classic Triad
       1. microvacuolation of cortex and gray matter termed **spongiosis**
       2. **cortical astrogliosis** and neuronal loss
       3. **Kuru plaques** – composed of aggregates of prion protein
- Prion protein
  - resistant to digestion of proteinase K
  - mutations identified in the familial form of spongiform encephalopathy
- Creutzfeldt-Jacob disease
  - 1 in 1,000,000 individuals
  - Clinical Manifestations
    - rapidly progressive dementia (3-6 months)
    - myoclonus
    - high voltage periodic EEG discharges
    - seizures
    - death at an average of 7 months after clinical presentation