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

<table>
<thead>
<tr>
<th>Most causative organism according to age:</th>
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</thead>
<tbody>
<tr>
<td>Neonate</td>
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<tr>
<td>Infants</td>
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<tr>
<td>Teens/ young adults</td>
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<tr>
<td>Elderly</td>
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• 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° 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 coxsackie virus
- CSF: lymphocytic pleocytosis, normal glucose, +/- inc. protein

**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

**EMPYEMA**
- Usually from infection of the sinuses or skull with contiguous spread to the subdural space
- **Complication**
  - Worst: S. Sagittal Sinus thrombosis 2° to infection of the vascular channel
  - Epidural abscess in the spinal cord
- **Causative agent**
  - Usually S. Aureus

**CHRONIC MENINGOENCEPHALITIS**
- **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
  ➢ obliteratorive 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 obliteratorive 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 2nd 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 temporoal lobes and orbital gyri
• lethargy, mood change, fever, seizures, 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 1st 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 1st infection
  ➢ progressive 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)

1ª HIV Meningoencephalitis
- AIDS dementia
- associated w/ memory loss, apathy, confusion
- MICRO
  - microglial nodules and reactive gliosis
- Vascular myelopathy of HIV
  - nearly identical to changes of Vit B₁₂ 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

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