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Introduction

- Potential infections:
  - Cerebral cortex --> encephalitis
  - Meninges --> meningitis
- Potential abscesses:
  - Cerebral cortex --> Brain abscess
  - Subdural Abscess --> (between arachnoid and dura)
  - Epidural Abscess
- Blood brain barrier prevents entry of invading pathogens and toxic substances. However:
  - Also prevents entry of Immunoglobulins, complement, and antibiotics.
    - Therefore, if pathogen crosses BB barrier, CNS infections progress fast and often serious.
    - Maximal doses ("meningeal doses") of abx are often required.

Meningitis

- See sub-page

Encephalitis

- See sub-page

Brain Abscess

- **Symptoms:**
  - MOST COMMON: Severe **headache** at site of abscess.
  - Sudden worsening = rupture of abscess into ventricles... high mortality rate (25-85%).
  - Many present with triad:
    - **Headache**
    - **Fever**
    - **Focal Neuro Deficit**
  - Other Symptoms based on location:
    - Neck stiffness only if occipital brain abscess or rupture into ventricle.
    - altered mental status, lethargy, coma.
    - Vomiting associated with increased CSF pressure.

- **Findings:**
  - Fever not present in 50%
  - Neuro findings are late.
  - Papilledema - late manifestation (25%)
  - CN VI and III palsies from high ICP.
  - Seizures if frontal brain abscess
- **Two causes:**
  - 1. Direct spread from middle ear, frontal sinus, or dental infection
  - 20-35% of patients --> do not find cause.
- **Cerebritis** (inflammation and edema) --> necrosis, fibrotic capsule formation.
- **Organisms:**
  - Organism provides clues on site of infection.
  - Anaerobic bacteria (mouth/genital tract)
    - Bacteroides fagilis, Prevotella, Propionibacterium, fusobacterium...
  - Aerobic gram- cocci (S. viridans, S. milleri, S. pneumo (rare), S. aureus)
  - Aerobic gram- rods --> usually with neurosurg
Immunocompromised:
- Toxoplasma, Nocardia, Aspergillus/cryptococcus/coccidioides.

Immigrants (parasites)
- Cysticercosis parasite (85% of brain infections in Mexico City)
- Entamoeba histolytica
- Schistosoma japonicum
- Paragonimus

Diagnosis:
- Space occupying lesion (SOL) suggested by:
  - Focal symptoms (even unilateral headache)
  - signs (neuro deficits)
  - papilledema
- LP CONTRAINDICATED, unless SOL excluded. (If papilledema or focal findings --> NO LP!!  CT first)
- MRI better than CT (more sensitivity in picking up lesions) (Diffusion weighted MRI help discriminate abscess vs. neoplasms). CT only if unable to do MRI.
  - Stages on CT:
    - Early cerebritis
      - irregular lesion of low density - no contrast enhancement.
    - Later cerebritis
      - Thick diffuse ring enhancement (enlarging) on contract injection.
    - Late cerebritis
      - Necrosis, Pre-contrast: ring of higher density surrounding edematous brain.
      - Contrast: thin ring, non-uniform in thickness.
    - Healed abscess
      - Collagen capsule becomes isodense. No enhancement on contrast.
- Treatment:
  - Neurosurg consult to drain abscess if >2.5cm lesion.
    - (Excision or stereotactic aspiration), culture specimens.
  - IV abx 6-8weeks
    - +/- prolonged oral therapy if appropriate agent is available.
    - (IV empiric therapy based on predisposing condition and presume pathogensis)
      - Generally:
        - Ceftriaxone (enterobactericiae) + metronidazole (anaerobic lytic due to mouth flora)
        - IF Dental Abscess: use penicillin + metronidazole to cover mouth flora
        - IF concerned of pseudomonas (neurosurg)
          - Use ceftazidime or cefepime
        - IF trauma (worry about S.aureus) add vancomycin (MRSA) or oxacillin/nafcillin (MSSA) depending on resistance patterns... aminoglycosides, erythromycin, tetracycline, 1st gen cefs also used.
        - IF hematogenous spread:
          - Typically vanco + gentamycin for empiric therapy.
  - Steroids:
    - if mass effect + mental status change.
    - IV dexamethasone (load 10mg then 4mg q6h)
    - Do not worry about immunocompromise...
    - DC as soon as possible.
      - Reduce contrast enhancement on CT (hard to monitor)
      - Decrease antibiotic penetration
      - Slow capsule formation (can rutupre into ventricles)
  - Repeat Neuroimaging
    - IMPORTANT*, every other week up to 3months after completing therapy.
    - To monitor for expansion of abscess or failure to respond.
- Prognosis:
  - Depends on stage:
    - 0–30% generally
    - 60–100% if stupor/coma
    - 80–100% if ruptures into ventricle.
Cranial Subdural Empyema

- Most common predisposing condition is in 40-80% of pts.
  - Organisms (in sinuses): Aerobic Streptococci, Staphylococci, Aerobic gram negatives, and Anerobic streptococci (+ other anerobes). Polymicrobial infection is common.
- Symptoms and signs:
  - Common: Rapidly progressive **headache** localized then generalized as progresses.
  - Increased ICP: nausea, vomiting etc..
  - Meningeal Irritation: meningitis-type symptoms.
  - Focal cortical inflammation
- Diagnosis:
  - MRI preferred to CT.
  - Better clarity of morphologic detail.
    - MRI better because:
      - Can see empyemas not seen on CT, esp those in base of brain, falx cerebri, and those in the posterior fossa.
      - Extra-axial empyemas from sterile effusions from subdural hematomas.
- Treatment:
  - Surgical emergency.
    - Decompress the brain and evacuate the empyema.
    - Often craniotomy (better than craniectomy or burr holes based on a study).
    - Empiric antimicrobial therapy with vancomycin, metronidazole and 3rd or 4rth cephalosporin.

Spinal Epidural Abscess

- Spinal canal has anterior and posterior epidural space
- Mechanism: of infection:
  - Spread from osteomyelitis or disk space
  - Spinal surgery or epidural catheter.
  - Hematogenous spread from:
    - Skin
    - UTI
    - IV drug use.
  - Organisms:
    - S. aureus (most common)
    - Can see GN’s or anaerobes if GU or GI source.
- 4 stages of clinical presentation:
  1. Back Ache and focal vertebral pain
  2. Nerve root pain (radiculopathy/parasthesias)
  3. Spinal Cord dysfunction
  4. Paraplegia
- Symptoms:
  - Low back pain, fever, radicular pain, lower motor deficits, cord compression signs, spinous process tenderness.
  - **Back pain + fever --> consider epidural abscess**
  - MRI is test of choice.
- Diagnosis:
  - MRI with Gadolinium --> procedure of choice!!!
    - Can see spinal cord + epidural space in saggital and transverse sections.
    - Can identify accompanied osteomyelitis, intra-medullary spinal cord lesions and diskitis.
- Treatment
  - **If spinal cord compression:**
    - URGENT surgery.
    - Can return function if done in 24-36hrs following neurological change.
      - Emergency surgical drainage.
  - Empiric Abx:
    - Usually anti-staphylococcal agent (cloxacillin, nafcillin, oxacillin etc..)
• Usually (in US and MKSAP) **vancomycin** for empiric MRSA coverage pending susceptibility testing. 
  (HIGH MRSA rates > 50% in some cases, vanco considered first line in US and MKSAP).
• PLUS **antipseudomonal cefalosporin** or **carbapenem** (for GN bacilli, esp for IVDU or spinal procedure).
  (I.e. MKSAP answer is vancomycin + ceftazidime)
  ▪ Usually need prolonged (4-6weeks) tx with nafcillin, oxacillin, metronidazole, ceftriaxone.
  ◦ Antimicrobial therapy alone can be considered in patients without long tract signs (i.e. if only pain and radicular symptoms), frequent follow-up, neuro exams, serial MRI studies to demonstrate abscess resolution are important.
  ◦ TB can be the cause.

**Generalized Neuropathy Causes**

**Botulism**

• Two types of exposures:
  ◦ Preformed Toxin:
    ▪ home-canned foods
  ◦ In-vivo toxin Production: (After ingestion and spore germination)
    ▪ Honey (infants)
    ▪ Wound contamination.
• **Symptoms** (1-5 days post ingestion) --> Classic Triad:
  ◦ Symmetric descending flaccid paralysis with prominent bulbar palsies:
    ▪ 4 D's of bulbar palsy:
      ▪ Diplopia
      ▪ Dysarthria
      ▪ Dysphonia
      ▪ Dysphagia
  ◦ Normal body temperature
  ◦ Clear sensorium
• **Diagnosis:**
  ◦ Toxin in serum, stool, gastric aspirate or suspect foods.
• **Treatment:**
  ◦ Supportive
  ◦ Passive immunization using trivalent equine antitoxin (A, B, and E).
  ◦ **MONITOR RESPIRATORY STATUS**

**Guillain-Barre Syndrome**

• Symptoms:
  ◦ Typically: Antecedent infection (gastroenteritis from Campylobacter)
  ◦ Ascending paralysis and parasthesias
  ◦ Can have oculomotor findings (like botulism).

**Paralytic Shellfish Poisoning**

• Ingestion of any type of filter-feeding molluscan shellfish (i.e. clams, oysters, scallops, muscles)
  ◦ Specific neurotoxin (saxitoxin) produced by algae accumulated.
• Symptoms hours to days post-ingestion
  ◦ Tinging of lips + tongue. ---> progresses to parasthesias of hand digits and feet.
  ▪ Eventually can lose control of hands and feet.
If lots of toxin ingested: thorax and abdo muscles can paralyze causing respiratory difficulty.

**Tick Paralysis**
- Associated with *Dermacentor* ticks (U.S. Pacific Northwest)
- Symptoms:
  - Ascending paralysis (proximal large muscles).

**Prion Diseases of CNS**
- Prions are novel, composed of transmissible proteins that lack genetic material.
- Cause 5 syndromes in humans.
  - Kuru
  - Gerstmann-Straussler-Scheinker Syndrome
  - Fatal Familial Insomnia
  - Sporadic Creutzfeldt Jakob Disease (two most common)
  - Variant Creutzfeldt-Jakob Disease

**Diagnosis:**
- Progressive neurologic impairment
- Absence of inflammatory CSF findings
- Presence of spongeform changes on neuropathologic exam (biopsy). [often post-mortem :(

- No treatments available... fatal.

**Creutzfeldt-Jakob Disease**
- Classified as:
  - Sporadic (most common) 85%
  - Familial
  - Iatrogenic (~1%)
  - Variant (~1%)
- Probable Sporadic CJD criteria

**WHO Probable CJD: (must meet all criteria)**
- 1. Progressive dementia
- 2. Clinical Signs
- 3. Lab or EEG findings
- 4. NO alternative diagnosis found on routine investigations.

- Clinically:
  - Psych symptoms, cognitive decline, motor dysfunction.
  - Extrapyramidal signs in >65%.
  - Myoclonus, rapidly progressive dementia are hallmarks on disease.
- Median survival after onset is 5 months.
- Labs:
  - Unrevealing.
  - CSF usually acellular (normal), maybe slight protein elevation.
  - **14-3-3 protein** - specific neuronal protein in CSF fluid is elevated = indirect marker of sporatic CJD.
    - Low Sn + Sp, only available in one lab.
  - EEG - some findings.
  - MRI - focal cortical hyperintensity on DWI or FLAIR = predictive of infection.
Neural biopsy - spongiform changes - histopathologic staining for PRCSC prion protein (usually made post-mortem)

- Surgical procedures discouraged - can contaminate surgical instruments... exposes healthcare workers.
  - Normal autoclaves do not remove prions!
  - Need special procedures.

**Variant Creutzfeldt-Jakob Disease**

- In 1990's cluster of cases in UK --> had variant CJD.
  - They were younger, psychiatric presentations, less rapid disease progression.
  - Found that this outbreak is unique.
- ON biopsy: heavy concentrations of amyloid plaque in cerebrum + cerebellum
  - Stain for a type of prion protein - **PRPSC Type 4** pattern in tonsillar tissue...unique. Allows premortem dx.
  - Consumption of beef during an epidemic of bovine spongiform encephalopathy supports animal to human transmission.

**Diagnosis:**
- Radiographic + neuropathologic exam.
  - MRI - pulvinar sign.
  - Identification of prion protein (on stains) in tonsillar tissue allowing for pre-mortem histopathologic diagnosis.

- Changes of animal feeding and butchering practices lead to decline in variant CJD.