CSF RHINORRHEA

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Basic Principle of CSF Rhinorrhea

- CSF rhinorrhea is the result of an osseous defect at the skull base coupled with a disruption of the dura mater and arachnoid with a resultant pressure gradient that leads to a CSF leak.
CSF Basics

- 50-80% produced by choroid plexus
- ~30% produced by ependymal surface

Production
- Result of capillary ultrafiltration
  - Regulated by Na\(^+\)/K\(^+\) ATPase activity
    - Na\(^+\) ions are taken into the epithelial cell from the vessel
    - Another Na\(^+\)/K\(^+\) ATPase on the ventricular side then pushes the Na\(^+\) out into the ventricle
    - Water follows the ions into the ventricle
    - Result is CSF
CSF Basics

- **Consistency**
  - Ions - $\text{Na}^+$, $\text{K}^+$, $\text{Mg}^{2+}$, $\text{Ca}^{2+}$, $\text{Cl}^-$, and $\text{HCO}_3^-$
  - Glucose (roughly 60-80% of blood glucose)
  - Water
  - Amino acids and proteins
  - Very few cells (polymorphonuclear and mononuclear cells)

- **Amount**
  - ~90-150mL of CSF at any one time
  - 20mL/hr is the normal production rate
  - 500mL/day produced
Etiology - Trauma

- Most common area - anterior cranial fossa (cribiform and roof of ethmoid)
- Non-surgical Trauma
  - ~80% of all CSF leaks result of blunt or penetrating head trauma
  - 2-3% of major head trauma results in CSF leaks
  - CSF leak in 15-30% of cases of skull base fracture
  - Leak may be either immediate (within 48 hours) or delayed
    - ~95% of cases of delayed leaks occur within 3 months
Etiology - Trauma

- Iatrogenic
  - 16% of CSF leaks
  - Endoscopic sinus surgery most common cause
    - 0.5% of ESS cases
  - Most common site of injury - lateral cribiform lamella
Etiology – Non-traumatic

- 4% of cases of CSF rhinorrhea
- **High Pressure Leaks**
  - 45% of non-traumatic cases
  - Sustained increased ICP -> Remodeling and thinning of the skull base -> Defect
    - Theorized to be due to ischemia from compression of vessels
  - Causes of Increased ICP
    - Tumor growth (typically pituitary tumors)
    - Hydrocephalus
      - Communicating or Obstructive
Etiology – Non-traumatic

- Normal Pressure Leaks
  - 55% of non-traumatic cases

- Causes
  - True Spontaneous leaks
    - Physiologic alterations in CSF pressure lead to point erosions in the skull base that can lead to defects
    - Every few seconds, normal elevations in CSF pressure up to 80 mmH₂O
    - Usually seen in adults
  - Tumors and other osteolytic causes
    - Tumors invade and erode skull base
      - Nasopharyngeal carcinoma, angiofibroma, inverting papilloma, osteomas
    - Other osteolytic lesions
      - Sinusitis
      - Syphilis
      - Mucoceles
Etiology – Congenital

- May have either increased ICP or normal ICP
- Failure of closure of the anterior neuropore -> herniation of meninges (encephaloceles)
  - Typically involves the foramen cecum and fonticulus frontalis
- Persistent craniopharyngeal canal
  - Vertical midline defect connecting the middle cranial fossa to the sphenoid sinus
Encephalocele

Persistent craniopharyngeal canal
Etiology – Congenital

- Empty Sella Syndrome
  - Sella turcica appears empty on imaging
  - Primary type
    - Congenital widening of the diaphragma sella + another event
      - Increased ICP transmitted through widened diaphragm -> causing compression of the pituitary
        - (Pseudotumor cerebri, intracranial tumors, hydrocephalus)
      - Rupture or displacement of cysts through the widened diaphragm causing compression
    - Increased pressure in sella thought to be cause of CSF leak
      - remodeling and thinning with eventual defect formation
Empty Sella Syndrome
Work-up – H&P

- **History**
  - Clear, watery discharge from a single nare
  - Supine positioning -> increased postnasal drip
  - Salty taste in mouth
  - Headaches relieved when CSF begins to drain

- **Physical**
  - Most cases = Exam unremarkable
  - Examine with nasal endoscopy
  - Have patient lean forward and strain – may elicit a leak
  - Compression of both jugular veins may elicit a CSF leak
    - Causes a rise in ICP
  - CSF rhinorrhea is typically clear, but if trauma has occurred, it may be mixed with blood
  - High likelihood of other injuries when trauma is involved (facial fractures, brain injury)
Diagnosis

- Halo or Ring Sign
  - Bloody CSF placed on a piece of filter paper
  - Blood will separate out from the CSF (central blood with clear ring)

- Dula et al found that the ring sign is not specific to bloody CSF
  - Blood mixed with water, saline, and other mucus will also produce a ring sign
Diagnosis – Laboratory Studies

- Glucose testing
  - Not very useful – False findings
    - Presence of blood -> Increased glucose readings (false positive)
    - Presence of meningitis or other intracranial infections -> Lower concentration of glucose in CSF (false negative)
  - Glucose oxidase paper
    - Changes color with glucose concentrations of 5+ mg/dL
      - False-positive results with lacrimal secretions or nasal mucus
        - Both contain enough glucose to cause paper to change color
  - If no blood present, may suspect CSF leak with a glucose concentration > 30mg/dL
  - Negative glucose virtually eliminates a diagnosis of CSF fluid
Diagnosis – Laboratory Studies

- Beta-trace protein
  - Found in CSF, heart, and serum
  - Not routinely ordered as it may be altered in many cases
    - Elevated with renal insufficiency, multiple sclerosis, cerebral infarctions, and some CNS tumors
  - If serum level is < 1.0 mg/L
    - Fluid with a concentration > 2.0 mg/L = Positive for CSF
    - Concentration < 1.5 mg/L = Not likely to contain CSF
  - Sensitivity and specificity not as high as Beta-2-transferrin
  - If test is available, can be accomplished in 15 minutes
    - Not readily available at UTMB
Diagnosis – Laboratory Studies

- **Beta-2-transferrin**
  - Protein produced by enzymes *only in CNS*
  - Test requires 0.5cc of fluid
  - Specimens should be refrigerated
    - If not, protein will become unstable at room temperature within 4 hours
    - If refrigerated, can last 3 days
  - Highly sensitive and specific for CSF
  - If available, can get results within 3 hours
    - Most places require “send-out” to test, so may take days to get results back
Diagnosis - Imaging

- High Resolution CT Scans
  - Bony defects, pneumocephalus, soft tissue masses, hydrocephalus
  - Should have 1mm cuts with axial, sagittal and coronal views

- CT Cisternography
  - Inject intrathecal contrast dye and obtain CT scan
  - More accurate
    - Especially those with active leaks
  - Sensitivity for detecting leaks drops from nearly 100% with active leaks to 60% with intermittent leaks
  - More invasive

- MRI
  - Soft tissue abnormalities and pooling of CSF (high signal intensity on T2 images)
  - Must utilize contrast to differentiate sinus inflammation from CSF fluid
  - More expensive
  - Not as good at defining bony defects
Diagnosis - Imaging

- Nuclear medicine tests (radionuclide cisternography)
  - How it works
    - Intrathecal injection of radioactive tracers (technetium-99, I-131, Indium 111)
    - Pledgets placed at areas suspected of leak and scintigrams of the skull are obtained
    - Pledgets are removed and measured for radioactive tracer
  - Drawbacks
    - Almost always requires an active leak
      - With active leaks detection rate is 70%
      - Inactive leak - 30-40% detection rate
    - Poor localization in most cases
    - Radioactive isotope is absorbed into the circulatory system and deposited into normal tissues
CT & CT Cisternography
Diagnosis – Intrathecal Dye

- Intrathecal injection of Fluorescein dye
  - Good at locating active CSF leaks
  - Inject a solution of 0.5%-10% Fluorescein dye and wait 30 minutes to examine patient
  - Most cases - Dye can be seen without filters
    - Smaller defects may require filters or black light
      - Place yellow filter over endoscope and blue filter over light source
  - Important to keep low concentration of Fluorescein; high doses can lead to severe side effects (500+mg)
    - Seizures
    - Pulmonary edema
    - Coma
    - Death
Fluorescein Dye
Treatment - Basic

- **Conservative vs. Surgical**
  - Traumatic leaks respond well to conservative management
  - Spontaneous leaks tend to require surgical correction

- **Basic Conservative Management**
  - Bed rest
    - 7-10 days
    - Head of bed 15-30 degrees
  - No’s:
    - Nose blowing
    - Straining - stool softeners
    - Coughing
    - Heavy lifting
  - 75-80% of traumatic CSF leaks will spontaneously resolve with this management
Treatment - Antibiotics

- Controversial
- Reason for use = Prevent intracranial infections
- Evidence
  - Brodie et al meta-analysis in 1997
    - 6 studies
    - 324 patients
      - 237 treated with antibiotics
      - 87 not treated with antibiotics
    - Meningitis
      - 2.5% of patients in the antibiotics group (6/237)
      - 10% of no-antibiotic group (9/87)
  - Villalobos et al meta-analysis in 1998
    - 12 studies
    - 1241 patients
      - 719 treated with antibiotics
      - 522 not treated with antibiotics
    - 1.34x more likely to develop meningitis without the use of antibiotics in cases of CSF leak from basilar skull fracture
- Risk of selecting out more virulent bacterial strains with use
Treatment - Diuretics

- Utilized in the presence of CSF leak with increased ICP
- Acetazolamide
  - Inhibits the conversion of water and CO$_2$ to bicarbonate and H$^+$
  - Loss of H$^+$ slows the action of the Na$^+$/K$^+$ ATPase enzymes that are responsible for the production of CSF -> Decreased ICP
Treatment – Lumbar Drain

- Consider if CSF leak does not resolve after 5-7 days of conservative management
- Continuous drainage is recommended over intermittent drainage
  - Prevents spikes in CSF pressure
- 10-15cc/hr
- Risks:
  - Headaches
  - Nausea and emesis
  - Pneumocephalus
  - Infection
  - Coma
Treatment - Surgical

- Intracranial Approach
  - When to use:
    - Comminuted skull fractures with displaced fragments requiring reduction
    - Extensive skull base fractures
    - Fractures associated with intracranial hemorrhages or contusions that require craniotomy for treatment
  - Dural defects may be closed primarily with or without the use of grafts
    - Free or pedicled periosteal or dural flaps
    - Muscle plugs
    - Mobilized portions of the falx cerebri
    - Fascia grafts
    - Many commercial grafts
  - Reinforce grafts with fibrin glue
Intracranial Approach – Advantages/Disadvantages

- **Advantages**
  - Direct visualization of defect
  - Inspection of adjacent cerebral cortex
  - Better chance of patching a defect in the face of increased ICP

- **Disadvantages**
  - Increased morbidity
  - Increased hospital time
  - Injury to brain from retraction (hematoma, seizures, cognitive dysfunction, risk of permanent anosmia)
  - Not good for visualization of sphenoid sinus
Treatment - Surgical

- Extracranial Approach
  - Most often endoscopic -> Success rates of 90+%
  - Advantages of endoscopic use
    - Better magnified visualization
    - Angled visualization
    - No external incisions
    - Minimizes intranasal mucosal injuries
Treatment - Surgical

- Endoscopic Repair
  - Good visualization and exposure = key
  - If an encephalocele is present
    - Cauterize stalk prior to reduction - prevents intracranial hemorrhage
  - 2-5mm of bone should be exposed around the defect
  - Grafts - 30% larger than the defect to account for shrinkage
  - Type of grafting material
    - Cartilage
    - Bone (septum, mastoid tip, middle turbinate)
    - Mucoperichondrium
    - Septal mucosa
    - Turbinate mucosa and/or bone
    - Fascia (temporalis, fascia lata)
    - Abdominal fat
    - Pedicled septal or turbinate flaps
      - Tend to tent, fold and contract, so not as good as free tissue use
Treatment - Surgical

- Grafting techniques
  - Important: All mucosa must be removed from the defect to ensure that a mucocele does not form
  - Overlay
    - Place graft directly over defect
  - Underlay
    - Place graft between dura and bony defect
  - Combined
    - Both underlay and overlay grafts
  - Fibrin glue -> provides improved seal
  - Gelfoam packing over the seal with or without nasal packing may further improve seal
  - Increased ICP -> Use multilayered grafting
Repair Based on Defect Size

- **Size of defect**
  - < 2mm – Almost any grafting technique is successful
  - 2-5mm – Can typically get away with just utilizing an overlay graft
    - Communited bone segments or significant dural injury
      - Composite graft
      - Separately harvested bone + mucosa
        - Bone placed in an underlay fashion
        - Mucosa placed in an overlay fashion
  - >5mm – Composite or separate bone+ mucosa grafts needed
Post-Operative Management

- Bed rest with HOB 15-30 degrees for 3-5 days
- Stool softeners
- Try to maintain normal BP
- No straining, coughing, heavy lifting
- If lumbar drain is utilized – 3-5 days in place
- Non-absorbable packing utilized - antibiotics
Sources