Treatment and Management of Venous Sinus Thrombosis

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• No actual or potential conflict of interest in regards to this presentation

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At the conclusion of this course participants will be able to

- Identify the epidemiology, pathophysiology and clinical features of cerebral venous sinus thrombosis (CVST)
- Analyze diagnostic modalities of CVST
- Evaluate principles of treatment of CVST
Case

- 35 year old healthy Female delivered a healthy infant via C-section
- 3-4 days later, she developed headaches
- Another 3 days later, friends found her confused on the floor with her baby next to her
- Later in the day had a witnessed episode of generalized shaking
Case

- Head CT at OSH shows cerebral sinus venous thrombosis
- Admitted, heparin drip started, transitioned to subcutaneous enoxaparin
- Had several odd episodes of generalized shaking while maintaining consciousness
- “Screaming in pain” with one of those episodes
- Repeat head imaging showed progression of CVST thrombosis despite anticoagulation
- Transfer to Rush
- Extensive dural venous sinus thrombosis involving the entire superior sagittal sinus, right transverse and sigmoid sinuses
- Partial thrombosis of the left transverse/sigmoid sinuses and several parasagittal cortical veins
Upon arrival to Rush:

- Somnolent, but easily arousable
- Complains of severe headache
- Fully oriented
- Intact cranial nerves
- Fundoscopy shows blurred disc margins
- Full motor strength throughout
- No sensory deficit

- Heparin gtt restarted
Next day:

- More somnolent, difficult to arouse, inattentive, non-verbal
- CN intact
- All 4 extremities drift to bed when she becomes inattentive, improves when stimulated

- Consulted endovascular team
  - Severe thrombosis of all the intracranial sinuses
  - Undergoes mechanical thrombectomy and partial recanalization of all sinuses
Case – MRI brain/ HCT
Case - Hospital Course

• Mental status and speech slowly improve over days
• Transitioned to coumadin
• Discharged to acute rehab

3 months later:
• Doing very well
• Neurologic exam is normal
• Headaches subsided 2-3 weeks after discharge

• Continues on warfarin, INR is therapeutic
• Levetiracetam for seizures, which have not recurred
Epidemiology, pathophysiology and clinical features of CVST
CVST - Epidemiology

• Cerebral venous thrombosis
  – Venous sinus thrombosis
  – Cortical vein thrombosis
• Relatively rare cause of stroke (<1%)
• Annual incidence estimated 3 - 7 cases per million
• Comparable incidence to acute bacterial meningitis in adults
• More common among young women and children
• Can cause devastating injury to the brain, but most patients have a good prognosis if it is recognized and treated early
Cortical veins 17%
Posterior frontal vein
Trolar vein
Anterior frontal vein

Superior sagital sinus 62%
Deep venous system 11%
Straight sinus 18%
Transverse (lateral) sinus 41-45%
Sigmoid sinus

% location of CVST
(International Study on Cerebral Venous and Dural Sinuses Thrombosis, n= 624)

Internal Jugular 12%
Thrombosis of the cortical veins:
- Localized vasogenic edema
- Venous infarction with cytotoxic edema
- Hemorrhage

• Symptoms:
  - Seizures
  - Focal neurologic symptoms

Samuels & Webb, NCS Practice Update 2013
Thrombosis of the large venous sinuses:
- Obstructs venous drainage
- Impaired CSF absorption through arachnoid villi
- Intracranial hypertension without hydrocephalus

• Symptoms:
  - Elevated intracranial pressure
  - Bi-hemispheric symptoms (stupor, coma)
CVST - Pathophysiology

- Multiple etiologic factors
- Usually one or more predisposing risk factors plus one inciting factor
- Thrombosis develops through common pathways of:
  - Hypercoagulability
  - Hemoconcentration
  - Direct injury or inflammation of the vessel
  - Venous stasis
- Transient and/or permanent risk factors raise suspicion for CVST and influence treatment duration
CVST - Transient Risk Factors

• Infections
  – Central nervous system (empyema, meningitis)
  – Ear, sinus, mouth, face and neck (otitis, mastoiditis, tonsillitis, stomatitis, sinusitis, cellulitis)
  – Systemic infections (sepsis, endocarditis, tuberculosis, HIV, malaria)

• Pregnancy and puerperium

• Physical precipitants
  – Head trauma
  – Lumbar puncture, myelography, intrathecal medications, spinal anesthesia
  – Radical neck surgery
  – Neurosurgical procedures
  – Jugular and subclavian catheters
CVST - Transient Risk Factors

- Drugs with prothrombotic action
  - Oral contraceptives
  - Hormone replacement therapy
  - Androgens
  - Medroxyprogesterone acetate
  - L-asparaginase
  - Cyclosporine
  - Tamoxifen
  - Steroids
  - Lithium
  - Thalidomide

- Ecstasy
- Sildenafil

- Other conditions
  - Dehydration
  - Diabetic ketoacidosis
## CVST - Permanent Risk Factors

### Prothrombotic conditions

<table>
<thead>
<tr>
<th>Genetic</th>
<th>Acquired</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein S, C, antithrombin deficiencies</td>
<td>Antiphospholipid AB syndrome</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Prothrombin mutations</td>
<td>Cyanotic congenital heart disease</td>
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</tbody>
</table>
CVST - Permanent Risk Factors

• Malignancy
  – Central nervous system (meningioma)
  – Solid tumors outside central nervous system
  – Hematological (leukemias, lymphomas)

• Hematological condition
  – Anemias (sickle cell disease and trait, iron deficiency, folic acid deficiency)
  – Paroxysmal nocturnal hemoglobinuria
  – Polycythemia (primary or secondary)
  – Thrombocythemia (primary or secondary)
CVST - Permanent Risk Factors

- **CNS disorders**
  - Dural fistulae

- **Inflammatory diseases**
  - Behçet’s disease
  - Systemic lupus erythematosus
  - Sjögren’s syndrome
  - Wegener’s granulomatosis
  - Temporal arteritis
  - Thromboangiitis obliterans
  - Inflammatory bowel disease
  - Sarcoidosis

- **Other disorders**
  - Thyroid disease
    - Hyperthyroidism
    - Hypothyroidism
CVST - Clinical Features

- Onset acute, subacute or chronic
- Headache is most common, nearly 90% of patients
- Other common presenting symptoms:
  - Focal or generalized seizure (40%)
  - Focal motor weakness (37%)
  - Encephalopathy or change in mental status (22%)
  - Vision loss (13%)
  - Diplopia (13%)
  - Stupor or coma (13%)
CVST - Clinical Features

• Papilledema in 25-30% of patients
• Thrombosis of the cavernous sinus produces a characteristic syndrome:
  – Orbital pain
  – Proptosis
  – Chemosis
  – Variable dysfunction of cranial nerves III, IV, V, and VI
Diagnosis of CVST
High degree of clinical suspicion is key to the diagnosis

- Head CT
- CT Venography (CTV)
- MRI/MRV
- Catheter Angiography (DSA)
CVST Diagnosis

Head CT

• Non-contrast head CT may be normal
• Cannot exclude a diagnosis of CVST
• Suspicious findings include:
  – Cerebral edema
  – Bilateral infarction
  – Infarction in a non-arterial distribution
  – Lobar intracerebral or subarachnoid hemorrhage
  – Hyperdense thrombosed cortical veins
  – Hyperdensities within the venous sinuses
CT Venography (CTV)

- Sensitivity of 95% compared with digital subtraction angiography, widely available, quick
- Less expensive than MRI
- Less invasive than conventional angiography
- Provides good visualization of the major venous sinuses
- Suboptimal for thrombosis in deep venous structures and cortical veins
- Radiation exposure and administration of intravenous contrast
CVST - Diagnosis

MRI/MRV

- MRI in combination with time-of-flight or contrast enhanced MR venography (MRV) → highly sensitive for the diagnosis CVST
- Abnormal T1 and T2 signal within the venous sinus and absence of normal flow through the venous sinus on MRV confirms the diagnosis
- Age of the thrombus determines T1 and T2 signal characteristics

Samuels & Webb, NCS Practice Update 2013
Catheter Angiography (DSA)

- CTV or MRI/MRV is usually adequate for the diagnosis or exclusion of CSVT
- DSA may be necessary for:
  - Identification of an isolated cortical vein thrombosis without venous sinus involvement
  - Diagnosis and characterization of dural arteriovenous fistula associated with a CVST
Learning Objectives

Treatment of CVST
CVST - Treatment

Anticoagulation

- Cornerstone of treatment for CVST
- Prevent extension of the thrombosis and support spontaneous thrombus resolution
- Indicated even in the presence of intracranial hemorrhage
“no new symptomatic cerebral hemorrhages. Anticoagulation proved safe, even in patients with cerebral hemorrhage”

Patients with ICH and CVST:
27 treated with IV heparin, 4 died (mortality 15%)
13 not treated with heparin, 9 died (mortality 69%)
“ICH is not a contraindication to heparin treatment”
• American Heart Association recommendations:

“...initial anticoagulation with adjusted-dose UFH or weight-based LMWH in full anticoagulant doses is reasonable, followed by vitamin K antagonists, regardless of the presence of ICH”
(Class IIa; Level of Evidence B)

“Continuation of oral anticoagulation with vitamin-K antagonists is reasonable for 3-6 months followed by antiplatelet therapy“
(Class IIa, Level B)

• Essentially identical recommendations from (now defunct) European Federation of Neurological Societies
Thrombolytics and Endovascular Treatment Options

- Numerous case reports using localized thrombolytics and mechanical clot disruption
- No controlled trials to establish efficacy or safety of these therapies
- Appropriate agent, dose, route of administration and clinical situation have yet to be defined
- Increased risk of intracranial hemorrhage is most commonly reported complication
- Thrombolytic and endovascular treatment should be limited to select patients who decline despite anticoagulation
- Should be performed only in centers with sufficient expertise in neuro-endovascular interventions
Seizures

• Most common in patients with
  – Focal edema
  – Venous infarcts
  – Intracranial hemorrhage

• Prophylactic anticonvulsants may be considered

• Duration of treatment depends on:
  – Seizure recurrence (unprovoked, 5% to 32% of patients)
  – EEG findings in follow-up
  – Tolerability of antiseizure drugs
Intracranial Pressure

- Intracranial hemorrhage, edema and infarction lead to localized mass effect
- Venous outflow impairment causes decreased CSF reabsorption, communicating hydrocephalus and intracranial hypertension
- Hyperosmolar therapy (mannitol, hypertonic saline) should be administered to patients at risk for cerebral herniation
- Acetazolamide is reasonable to reduce CSF production
- CSF diversion (lumbar puncture, ventriculostomy) or optic nerve decompression can be effective if there is progressive visual loss
- Resection of hemorrhagic infarction or decompressive craniectomy may be required
- Anticoagulation should be resumed as soon as possible following surgical intervention
• Recanalization
  – At 3 months → 84%
  – At 1 year → 85%
  – Highest recanalization rates in deep cerebral veins and cavernous sinus thrombosis, lowest in lateral sinus thrombosis

• In adults, recanalization of the occluded sinus is not related to outcome

Saposnik et al., Stroke. 2011;42:1158-1192
CVST - Outcome

• 3% to 15% of patients die in the acute phase
• Patients at risk:
  – Depressed consciousness
  – Altered mental status
  – Thrombosis of the deep venous system
  – Right hemisphere hemorrhage
  – Posterior fossa lesions.
• Main cause of acute death with CVT is transtentorial herniation due to large hemorrhagic lesion
• Second is herniation due to multiple lesions or to diffuse brain edema.
• Status epilepticus, medical complications, and PE are other causes

Saposnik et al., Stroke. 2011;42:1158-1192
• 79% of patients will have complete recovery
• 9.7% are functionally dependent (mRS 3 or greater)
• 50% of survivors feel depressed or anxious, minor cognitive or language deficits may preclude them from resuming previous jobs
• Abulia, executive deficits, and amnesia result from thrombosis of the deep venous system, with bilateral panthalamic infarcts
• Memory deficits, behavioral problems, or executive deficits may persist
Questions?