Cerebral Venous Thrombosis (CVT)

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EPIDEMIOLOGY

・ 0.5-1% of all strokes.
・ female-to-male ratio 1:293:1
・ any age (newborn to elderly patients), 80% patients are < 50 yrs; age distribution:
  - men - uniform age distribution;
  - women - 61% aged 20-35 yrs (may be related to pregnancy or oral contraceptives)
・ mean age at presentation is nearly 1 decade younger in women compared to men (34 years vs. 42 years).

Age and sex distribution of cerebral venous and sinus thrombosis (CVT) in adults:

ETOLOGY

1. Infection: extension from paraanalar sinuses, middle ear (via emissary veins), face, oropharynx
   ← SUPERFICIAL, INTRACRANIAL, THROMBOPHLEBITIS
   N.B. orbital veins (drain from middle third of face, including paraanalar sinuses) have no valves - allow infection passage both arteriole and retorograde!
   • may be associated with epidural abscess, subdural empyema, meningitis, cranial osteomylitis.
   • frontal sinuses are most common source.
   • most commonly - LATERAL, and CAVERNOUS SINUSES.
   • Staphylococcus aureus is most common.

2. Trauma: 1) mild closed injury + depressed skull fracture (occules dural sinus) 2) iatrogenic - dural taps, infusions into internal jugular vein.

3. Tumors: - local compression, hypercoagulable state, antineoplastic drugs (e.g. tamoxifen, L-asparaginase).

4. Hypercoagulable states (present in 21% cases)
   1) antiphospholipid and anticardiolipin antibodies, protein S and C deficiencies, antithrombin III deficiency, lupus anticoagulant, Leiden factor V mutation, hyperhomocysteinemia
   2) parovosomal neuronal hemoglobinuria, thrombotic thrombocytopenic purpura, sickle cell disease, polycythemia
   3) pregnancy and puerperium!!
   4) disseminated malignancies (paraneoplastic hypercoagulation)
   5) sarcoidosis, inflammatory bowel diseases (Crohns), collagenoses (incl. corticosteroids used in treatment)
   6) vasculitis (such as Behcet syndrome).
   7) septicemic syndrome, hepatic cirrhosis.
   8) dehydration, cachexia (“marantic” thrombosis in infancy) - superior sagittal sinus is most common.

5. Medications: oral contraceptives (incl. 3rd-generation), corticosteroids; e-aminoacapric acid, L-asparaginase; heparin (thrombotic thrombocytopenia with venous sinus thrombosis).

PATHOPHYSIOLOGY

Cerebral venous thrombosis is uncommon cause of cerebral infarction (relative to arterial disease).
Symptoms related to cerebral venous and dural sinus thrombosis

Clinical patterns

1. **Superior sagittal sinus thrombosis** (70%; but less common site of infective thrombosis) – unilateral parasagittal more or less symmetric infarcts – most severe damage?
2. **Transverse (lateral) sinuses**
3. **Cavae sinus**
4. Inferior sagittal sinus, straight sinus, petrosal sinuses, vein of Galen – usually involved by secondary extension.
5. **Superior petrosal sinuses**

MRV showing the most frequent (%) location of cerebral venous and sinus thrombosis, as reported in the International Study on Cerebral Venous and Dural Sinus Thrombosis (n=624):

<table>
<thead>
<tr>
<th>Location</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Superior sagittal sinus</td>
<td>62%</td>
</tr>
<tr>
<td>Deep venous system</td>
<td>18%</td>
</tr>
<tr>
<td>Transverse (lateral) sinus</td>
<td>41-45%</td>
</tr>
<tr>
<td>Sigmoid sinus</td>
<td>12%</td>
</tr>
<tr>
<td>Superior petrosal sinus</td>
<td>5%</td>
</tr>
</tbody>
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Venous infarcts do not conform to arterial territories, are often hemorrhagic and multifocal.

### CLINICAL FEATURES

- Course is more severe in septic thrombosis.
- Course is mildest in isolated cortical vein thrombosis.

### 1. Signs of ICP ↑ (irreparable venous outflow)

- **Headache** – most common symptom! (90%); diffuse, increases over several days; thunderclap headache indicates associated SAH!!
- **Nausea & vomiting**
- **Normal or decreased level of consciousness** (may progress to coma)
- **Papilledema**
- **Distention of the scalp veins** may be noted.

### 2. Facial neurological deficit (focal brain injury from venous ischemia/infection or hemorrhage; 75% patients) – depending on area involved as thrombus extends to cortical veins (CN syndromes, hemiparesis, facial weakness, aphasia, ataxia, hemianopia, deafness, etc.).

- N.B. focal neurologic signs may be entirely absent with ICP ↑ pressure as only presenting sign!
- **Seizures** are more common (40%) than in arterial strokes!; can be recurrent.
- **Bilateral** brain involvement is not infrequent.

**Clinical patterns:**

- a) ISOLATED INTRACRANIAL HYPERTENSION (mimicking pseudotumor cerebri)
- b) FOCAL NEUROLOGICAL SIGNS (simulating arterial strokes or seizures)
- c) CAVERNOUS SINUS SYNDROME.

### Symptoms related to area of thrombosis:

#### Superior sagittal sinus thrombosis

- **Weakness in lower extremity** (unilateral or paraparesis) → hemiparesis (secondary to clot extension into cerebral veins)
- in infants – forehead edema, vein engorgement in area of anterior or posterior fontanel (caput medusae).
- bilateral involvement can produce **status** early in course.
- seizures in ~5% patients.
- course is frequently fulminating and prognosis guarded, although complete recovery may occur.

#### Lateral sinus thrombosis

- usually secondary to pediatric otitis media and mastoiditis (most patients are febrile with earache).
- swelling over mastoid region with distention of superficial veins.
- **Greissinger sign** - mastoid emissary vein thrombosis due to thrombus extension from sigmoid sinus.
- **Pseudotumor cerebri** – like picture (ICP ↑) – more common with right sinus occlusion (in most individuals, right sinus drains greater portion of brain).
- may produce **OTITIC HYDROCEPHALUS**
- most common focal sign – CN6 palsy.

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CEREBRAL VENOUS THROMBOSIS

- extension into jugular bulb → tenderness over jugular vein in neck, JUGULAR FORAMEN SYNDROME (Vernet) CN 9-11

LAYERS/NOUS SINUS THROMBOSIS

- septic thrombosis (S. aureus 66%) is associated with bacterial sinusitis (sphenoidal or ethmoidal) or orbital cellulitis; nonseptic thrombosis is rare!
- involves only one sinus at onset but rapidly spreads (via circular sinus) to opposite side.
- onset is usually sudden and dramatic - patient appears acutely ill with fever; > ½ patients have change in mental status.
- cranial nerve palsies (compressive phenomenon) → variable ophthalmoplegia (esp. early CN6 palsy), ptosis, decreased sensation in CN5-7 2 divisions.
- obstruction of ophthalmic veins → periorbital edema (1), proptosis, chemosis, papilledema with hemorrhages around disc; orbits are painful to pressure.
- septic thrombosis has high mortality.

DIAGNOSIS

IMAGING

MRI

- acutely sinus walls appear convex
- intensity follows blood intensity in ICH
- absence of flow void in venous channels.

N.B. acute thrombosis can appear hypointense on spinT2 (mimics flow void!!!); slow flowing blood may appear bright (mimics thrombus); H: MRV

1) absense of flow void in venous channels.

2) edema and infarct (unilateral or bilateral or single or multifocal) that does not follow distribution of expected arterial occlusion.

3) hemorrhagic infarction is commonly found (because of increased pressure in draining veins).

4) chronic organizing thrombus develops significant neovascularity - enhances strongly demonstrating "frayed" or "shaggy" appearance.

Transverse sinuses thrombosis:

A. Unenhanced coronal TI-MRI - high signal in right cerebellar hemisphere due to hemorrhage; absence of flow void and high signal in right transverse sinus (arrow). 

B. Enhanced coronal TI-MRI - hemorrhagic infarct better defined and thrombus in right transverse sinus (arrow) is demarcated by enhancing walls of sinus.

MRV

- excellent method of visualizing dural venous sinuses and larger cerebral veins.
- single-slice phase-contrast angiography (SSPCA) takes < 30 seconds and provides rapid and reliable information (depicts only flow and not thrombus) - procedure of choice in diagnosing CVT (specificity and sensitivity 100%).

N.B. TRANSVERSE SINUS flow gaps (in nondominant or codominant transverse sinus) should not be mistaken for thrombosis.

"empty delta" sign; note prominent sulcal enhancement caused by collateral venous drainage (mimics meningitis).

9-22A. Axial NECT scan in a 20-year-old engorged woman with headache, papilledema shows hyperdense right TI compared to the left sigmoid sinus; 9-22B. Sagittal T1WI in the same patient shows a normal "flow void" to the straight sinus. The XSS shows an abnormal "flow void" and -compare for the CSS -Oss bone grades & 90°- appear "filled with clot", that is almost isointense with brain.

9-22C. Axial T1WI in the same patient shows an enlarged right TI that appears filled with isointense clot. Compare with the normal "flow void" in the left vein of Labbe and transverse sinus (T; 9-22B). Axial T1WI in the same patient shows that the thrombosed right TI appears very hypointense and expands the "flow void" of the patent left TI (9-22D and note of Labbe).
Cerebral Venous Thrombosis

Late acute DST:
- May be normal!
- may show evidence of infarction (edema) that does not correspond to arterial distribution.

- useful in ruling out other conditions – neoplasm, subdural empyema, sinusitis.
- demonstration of infarct may be delayed up to 48-72 hours.
- hemorrhagic infarction:
  - parasagittally located - SUPERIOR SAGITTAL SINUS;
  - centrally located - STRAIGHT SINUS;
  - temporal located - TRANSVERSE and SMOID SINUSES.

- empty △ sign on contrast CT (most specific CT finding) - nonenhanced thrombus in SUPERIOR SAGITTAL SINUS surrounded by enhancement of engorged collateral veins around sinus and in sinus walls.
- dense triangle sign - fresh coagulated blood in SUPERIOR SAGITTAL SINUS.
- cord sign - thrombosed cortical vein.

Axial CT - cavernous sinus (CS) is distended, with abscess (arrowheads); stenosis of intracavernous ICA is response to abscess.

- normal dura and circulating blood are mildly hyperdense compared to brain on CT scans, so subtle increased attenuation of venous thrombi can be difficult to detect.
- venous sinuses lie directly adjacent to skull, so clots can also be obscured by attenuation artifacts.

"empty delta" sign - enhancing dura surrounding nonenhancing thrombus.
CEREBRAL VENOUS THROMBOSIS

Hyperdensity of right transverse sinus:

- equivalent to (or better than) MRV in identification of dural sinus thrombosis.

**CT V:****
- with delayed filming technique (to visualize venous system) - was procedure of choice prior to advent of MRV.
  - indicated only if MR studies are not diagnostic
  - intraluminal filling defects, flow absent within dural sinus.
  - delayed-emptying of cortical veins appear as if they are “hanging in space”.
  - narrowing of intracavernous ICA in CAVEROUS SINUS thrombosis.
  - direct venography - passing catheter from jugular vein into TRANSVERSE SINUS.
  - orbital venography is most definitive method for CAVEROUS SINUS thrombosis.

**ANGIOGRAPHY:**
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**OTHER STUDIES**

**EEG:**
- normal to mild generalized slowing or focal abnormalities.

**LUMBAR PUNCTURE:**
1) evaluation for meningitis
2) compression of jugular vein unilaterally with pressure measurement (now rarely used) → pressure? If contralateral TRANSVERSE SINUS is thrombosed (collateral circulation or incomplete compression of jugular vein may yield false-negative result); elevation of intracranial venous pressure may precipitate herniation!
  - CSF may be bloody or xanthochromic with parameningeal inflammatory profile and pressure↑.

**FUNDUSCOPY:**
- papilledema.

**BLOOD:**
- CBC - leucocytosis (sepsis), polycythemia, platelet count ↓ (thrombotic thrombocytopenic purpura).
  - D-dimer > 500 ng/ml may be beneficial in screening headache patients in ED - D-dimers are positively correlated with thrombosis extent and negatively correlated with symptom duration
    - sensitivity = 87.1%, negative predictive value = 99.6%, specificity = 91.2%, positive predictive value = 55.7%.

Hypercoagulable workup:
Anatomic variants of normal venous anatomy may mimic sinus thrombosis:
1. sinus atresia/hypoplasia
2. asymmetrical sinus drainage (20% of population has partial or complete absence of 1 lateral sinus)
3. prominent arachnoid granulations
4. intraparenchymal versus intrasinus septa.

Intracranial hemorrhage that occurred as the consequence of CVST is not a contraindication for anticoagulation. Endovascular therapy may be considered in patients with absolute contraindications. Anticoagulation may be considered, with a target INR of 2.0 for patients with recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia.

Supportive treatment during future pregnancies and the postpartum period is probably recommended (Class IIa; Level of Evidence B).

**TREATMENT**

**AH/A/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):**

- initial anticoagulation with adjusted-dose UFH or weight-based LMWH in full anticoagulant doses is reasonable, followed by vitamin K antagonist, regardless of the presence of ICH (Class IIa; Level of Evidence B).
- patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists may be continued for 6-12 months, with a target INR of 2.0-3.0 (Class IIb; Level of Evidence C).
- for patients with recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia, indefinite anticoagulation may be considered, with a target INR of 2.0-3.0 (Class IIb; Level of Evidence C).

**CVT during pregnancy**

**AH/A/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):**

- treat with full dose LMWH rather than UFH (Class IIa; Level of Evidence C).
- LMWH in full anticoagulant doses should be continued throughout pregnancy, and LMWH or vitamin K antagonist with a target INR of 2.0-3.0 should be continued for at least 6 weeks postpartum (for a total minimum duration of therapy of 6 months) (Class I; Level of Evidence C).
- future pregnancy is not contraindicated (Class IIa; Level of Evidence B); prophylaxis with LMWH during future pregnancies and the postpartum period is probably recommended (Class IIa; Level of Evidence C).

**ANTIBIOTICS** for septic thrombosis (empirically start with antistaphylococcal a/b):
- for CAVERNOUS SINUS thrombosis: **NAPOLIDIN or VANCOMYIN + METRONIDAZOLE +** 3rd-generation cephalosporin.

**MEDICAL**

1. HYDRATION
2. ANTICOAGULATION in therapeutic doses ASAP (Heparin → warfarin INR goal of 2-3) even if hemorrhagic infarction is present!!!!!!!!!

Cerebral Venous Thrombosis 

- LMWH may be preferable to unfractionated heparin.
- duration: for unprovoked thromboses: 6-12 months → reimagine and decide for continued anticoagulation; if patient is prothrombotic, duration is indefinite.
- may be followed with aspirin (role unclear).

**AH/A/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):**

- in patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists may be continued for 3-6 months, with a target INR of 2.0-3.0 (Class IIb; Level of Evidence C).
- in patients with unprovoked CVT, vitamin K antagonists may be continued for 6-12 months, with a target INR of 2.0-3.0 (Class IIb; Level of Evidence C).
- for patients with recurrent CVT, VTE after CVT, or first CVT with severe thrombophilia, indefinite anticoagulation may be considered, with a target INR of 2.0-3.0 (Class IIb; Level of Evidence C).

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3. **ANTIBIOTICS** for septic thrombosis (empirically start with antistaphylococcal a/b): for CAVERNOUS SINUS thrombosis: **NAPOLIDIN or VANCOMYIN + METRONIDAZOLE +** 3rd-generation cephalosporin.

4. Supportive treatment similar to arterial stroke (esp. reducing ICP, anticonvulsants)*. *remit seizure prophylaxis is not recommended (Class III; Level of Evidence C).
CEREBRAL VENOUS THROMBOSIS

THROMBOLYSIS at present is limited to specialized centers but should be considered for patients with significant deteriorating deficits.

- all studies concerning use of thrombolytics in CVT involve intrasinus administration - either direct instillation into sinus (at time of surgery) or use of microcatheters to reach venous sinus; i.e. no data about systemic IV effects for CVT.

- recent report describes use of rheolytic catheter device - delivers 6 high-velocity saline jets through halo device at catheter tip → Bernoulli effect breaks up thrombus, particulate debris is directed into effluent lumen for collection into disposable bag.

AHA/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):

steroids are not recommended, even in the presence of parenchymal brain lesions on CT/MRI, unless needed for another underlying disease (Class III; Level of Evidence B)

- steroids (may have a role in CVT by decreasing vasogenic edema, but steroids may enhance hypercoagulability) cause 4.8-fold increased odds of death or dependence (95% CI 1.2 to 19.8).

SURGICAL

AHA/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):

- endovascular intervention may be considered if deterioration occurs despite intensive anticoagulation treatment (Class IIb; Level of Evidence C).

- in patients with neurological deterioration due to severe mass effect or intracranial hemorrhage causing intractable intracranial hypertension, decompressive hemicraniectomy may be considered (Class IIb; Level of Evidence C).

OPEN THROMBECTOMY and LOCAL THROMBOLYTIC THERAPY – salvage therapy only for severe neurological deterioration* (despite adequate anticoagulation).

- surgery is indicated for septic thrombosis if no response to antibiotics in 24 h – remove infected bone (e.g. mastoidectomy), expose and drain sinus; ligate jugular vein (for LATERAL SINUS thrombosis).

PROGNOSIS

Mortality:

- untreated cases – 13.8-48%;
- treated cases – 12.5% (7% in acute phase, 1% during one year follow-up).

Full recovery:

- untreated cases – 29%;
- treated cases – 62.5%.

Morbidity:

- episodic headaches 11-30%
- seizures 8.8-10%
- pyramidal signs 11.7%
- visual deficits 5.9%
- aphasia 9%
- memory deficit and depression 17.6%

- some spontaneously recanalize.
- some form dural AVF.
- 59% (esp. males, polycythemia) developed recurrent thrombotic events.
- prognosis is worse in septic thrombosis.

FOLLOW UP

AHA/ASA Scientific Statement on Cerebral Venous Thrombosis (2011):

follow-up CTV or MRV at 3 to 6 months after diagnosis is reasonable to assess for recanalization in stable patients (Class IIa; Level of Evidence C).

BIBLIOGRAPHY for ch. “Neurovascular Disorders” ⇒ follow this LINK >>