Cerebral Venous Thrombosis (CVT)

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- thrombosis of venous sinuses, superficial or deep cerebral veins.

EPIDEMIOLOGY

- 1% of all strokes.
- **female**-to-male ratio 1.29-3 : 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).

ETIOLOGY

1. **Infection** extension from **paranasal sinuses, middle ear** (via emissary veins), **face**, **oropharynx** → SUPPURATIVE INTRACRANIAL THROMBOPHLEBITIS.
   N.B. orbital veins (drain from middle third of face, including paranasal sinuses) have no valves - allow infection passage both *anterograde* and *retrograde*!
   - may be associated with epidural abscess, subdural empyema, meningitis, cranial osteomyelitis.
   - 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 (occludes dural sinus)
   2) iatrogenic - dural taps, infusions into internal jugular vein.

3. **Tumors** (e.g. meningioma, neuroblastoma).

4. **Hypercoagulable states**:
   1) antiphospholipid syndrome, protein S and C deficiencies, antithrombin III deficiency, lupus anticoagulant, Leiden factor V mutation.
   2) paroxysmal nocturnal hemoglobinuria, thrombotic thrombocytopenic purpura, sickle cell disease, polycythemia.
   3) **pregnancy and puerperium**!!!
   4) disseminated malignancies (paraneoplastic hypercoagulation)
   5) sarcoidosis, inflammatory bowel diseases (Crohn), collagenoses (incl. corticosteroids used in treatment).
   6) vasculitis (such as Behcet syndrome).
   7) nephrotic syndrome, hepatic cirrhosis.
   8) dehydration, cachexia ("marantic" thrombosis in infancy) - superior sagittal sinus is most common.

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

PATHOPHYSIOLOGY

Cerebral venous thrombosis is uncommon cause of cerebral **infarction** (relative to arterial disease).

venous strokes : arterial strokes ≈ 1 : 62.5

- venous occlusion → tissue congestion → early severe VASOGENIC BRAIN EDEMA → VENOUS INFARCTION → CYTOTOXIC EDEMA:
  venous sinus thrombosis - infarction in cortex and adjacent white matter;
  deep cerebral vein thrombosis - infarction in basal ganglia, thalamus.
- venous sinus system itself lacks valves, permitting retrograde propagation of clots - thrombosis from **dural sinuses** may progress (esp. in septic thrombosis) to **cortical veins**.
  – obstruction of cortical veins (e.g. vein of Labbé) can produce significant damage.
  – although unusual, cortical vein thrombosis may be seen in absence of dural sinus involvement.
- back-transmission of high pressure into capillary bed usually results in significant ***hemorrhagic component***.
- **SAH** also may be presenting feature (due to venous hypertension).
  – CVT should be considered in workup of SAH, esp. when basilar cisterns are not involved!
- *if sinus occlusion occurs gradually* (as by neoplastic invasion), collateral drainage routes (incl. scalp veins) are recruited, thus avoiding cerebral edema and ICP↑.
- venous thrombi are ***rich in RBCs and fibrin*** but poor in platelets ("red thrombus") → replaced by fibrous tissue with time.

Venous infarcts *do not conform to arterial territories*, are often *hemorrhagic* and *multifocal*.

Frequency:
1) SUPERIOR SAGITTAL SINUS (70%, but less common site of infective thrombosis) – bilateral parasagittal more or less symmetric infarcts – most severe damage!
2) TRANSVERSE (LATERAL) SINUSES
3) CAVERNOUS SINUS
4) inferior sagittal sinus, straight sinus, petrosal sinuses, vein of Galen - usually involved by secondary extension.

CLINICAL FEATURES

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

1. **Signs of ICP↑:**
   1) **headache** - most common symptom!; increases over several days; thunderclap headache (usually indicates SAH) may be seen in sinus thrombosis!!!
   2) **nausea & vomiting**
   3) **normal ÷ decreased level of consciousness** (may progress to coma).

2. **Focal neurological deficit** (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 than in arterial strokes!; can be recurrent.

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 fontanels (caput medusae).
- bilateral involvement can produce ***stupor*** early in course.
- seizures in > ½ patients.
- course is frequently fulminant 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.
- **GRIESINGER 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***.
- **extension into jugular bulb** → tenderness over jugular vein in neck, JUGULAR FORAMEN SYNDROME (Vernet): CN 9-11

CAVERNOUS 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 $CN5_{1-2}$ divisions.
- ***obstruction of ophthalmic veins*** → periorbital edema (!), proptosis, chemosis, papilledema with hemorrhages around disc; orbits are painful to pressure.
- *septic thrombosis has high mortality.*

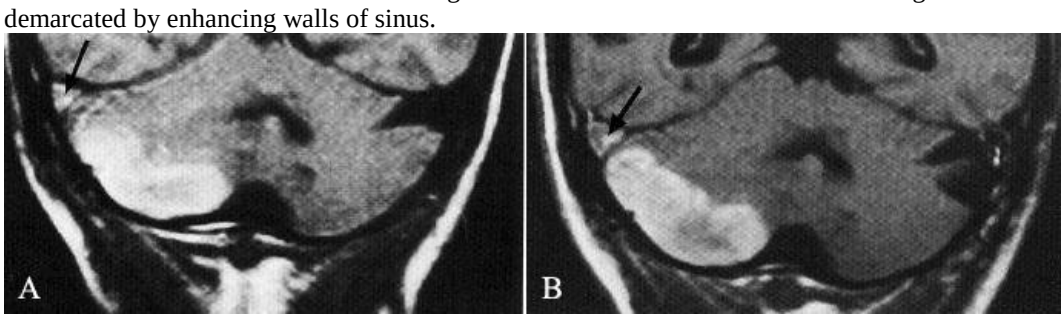
DIAGNOSIS

MRI

- acutely sinus walls appear convex
- intensity follows blood intensity in ICH

1) absence of flow void in venous channels.
   N.B. *acute thrombus* can appear hypointense on spinT2 (mimics flow void!!!); *slow flowing blood* may appear bright (mimics thrombus); H: MRV
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.

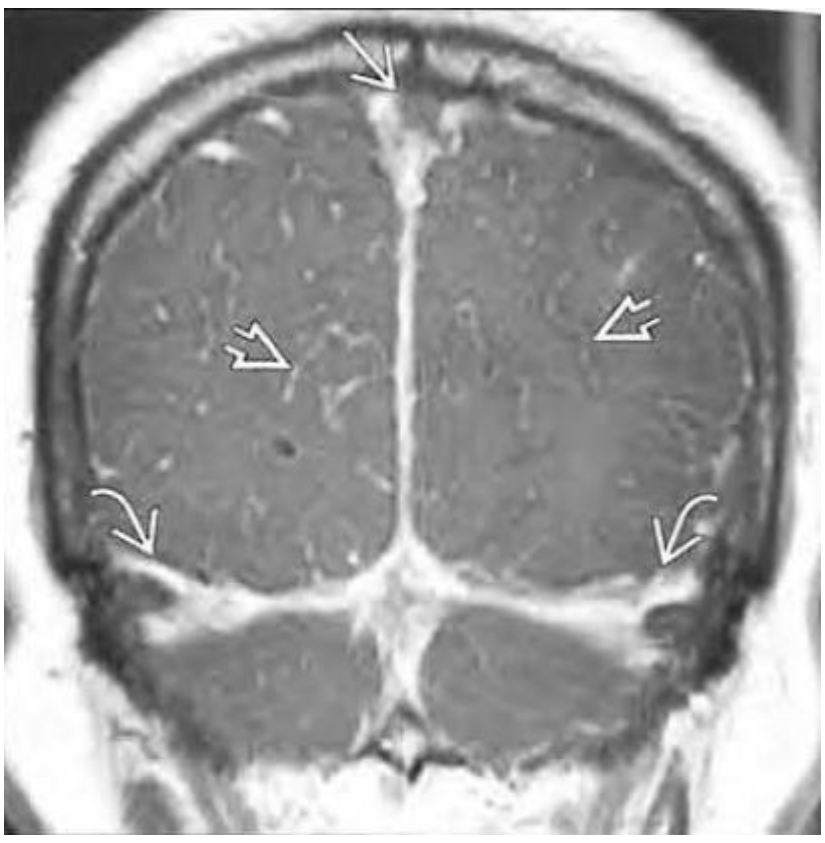
Transverse sinus thrombosis:
A. Unenhanced coronal T1-MRI - high signal in right cerebellar hemisphere due to hemorrhage; absence of flow void and high signal in right transverse sinus (*arrow*).
B. Enhanced coronal T1-MRI - hemorrhagic infarct better defined and thrombus in right transverse sinus (*arrow*) is demarcated by enhancing walls of sinus.

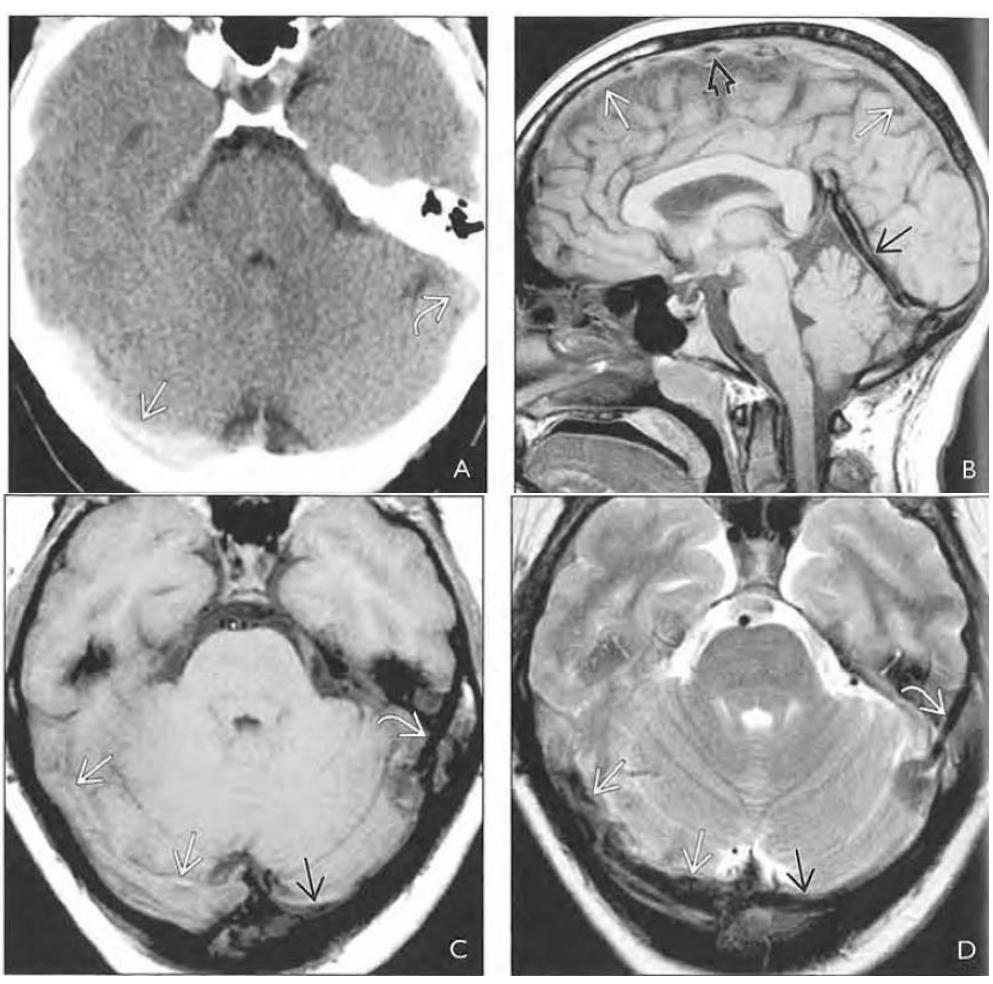


MRV

- 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):

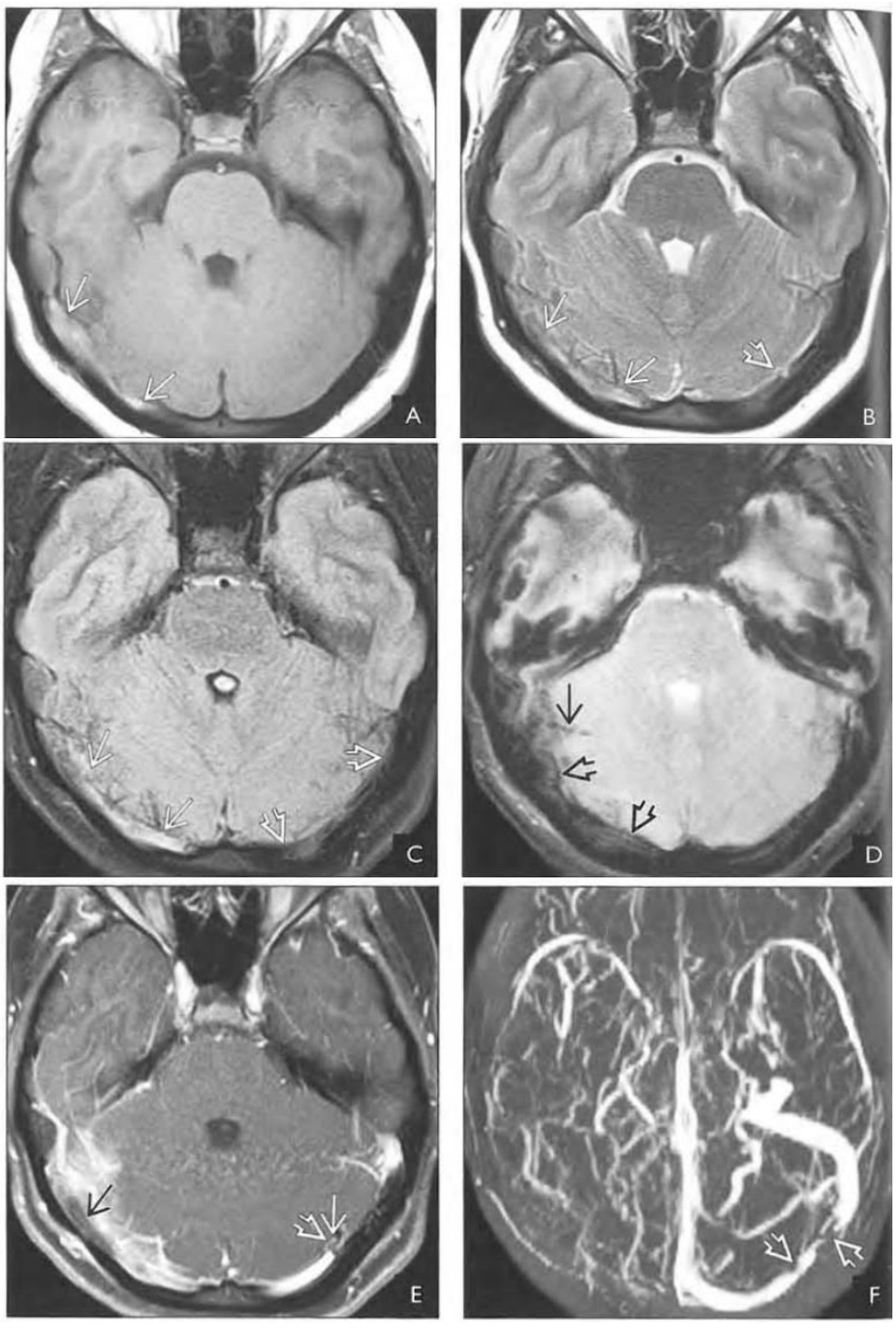




9-22A. *Axial NECT scan in a 29-year-old pregnant woman with headaches, papilledema shows hyperdense right TS compared to the left sigmoid sinus.* ***9-22B.*** *Sagittal T1WI in the same patient shows a normal "flow void" in the straight sinus. The SSS shows an absent "flow void" and—except for the CSF-filled arachnoid granulations—appears filled with clot that is almost isointense with brain.*

9-22C. *Axial T1WI in the same patient shows an enlarged right TS that appears filled with isointense clot. Compare to the normal "flow void" in the left vein of Labbé and transverse sinus.* ***9-22D.*** *Axial T2WI in the same patient shows that the thrombosed right TS appears very hypointense and mimics the "flow voids" of the patent left TS and vein of Labbé.*

Late acute DST:



9-25A. *Late acute DST in a 25-year-old man with several days of diarrhea and progressively worsening headache. NECT scan had demonstrated no definite abnormality. Axial T1WI shows mild hyperintensity in the right TS.* ***9-25B.*** *Axial T2WI shows that the thrombus in the right TS is beginning to appear mildly hyperintense, unlike the very hypointense clot seen on T2WI in acute DST. Note small T2 hyperintensity in the left TS.*

9-25C. *Axial FLAIR scan in the same patient shows that the right TS thrombus is mildly hyperintense. Contrast this with the normal "flow void" in the left TS.* ***9-25D.*** *Axial T2* GRE in the same patient shows "blooming" thrombus in the right TS and tentorial venous tributaries.*

9-25E. *Axial T1 C+ FS scan shows the nonenhancing thrombus in the right TS surrounded by the intensely enhancing dura. The left TS shows an ovoid filling defect with CSF intensity containing a linear central enhancing vein. Findings are characteristic of an arachnoid granulation.* ***9-25F.*** *Axial MIP of 3D TOF MRV shows nonfilling of the right transverse and sigmoid sinuses. The 2 ovoid filling defects in the left TS are arachnoid granulations.*

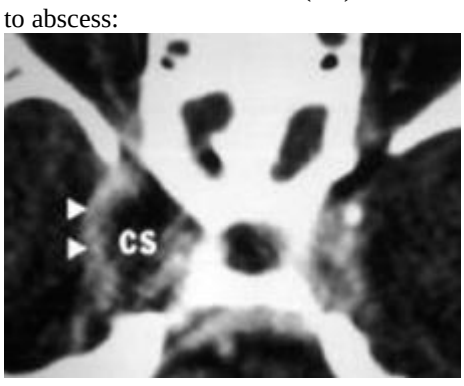
CT

May be normal!

- may show evidence of infarction (edema) that does not correspond to arterial distribution.

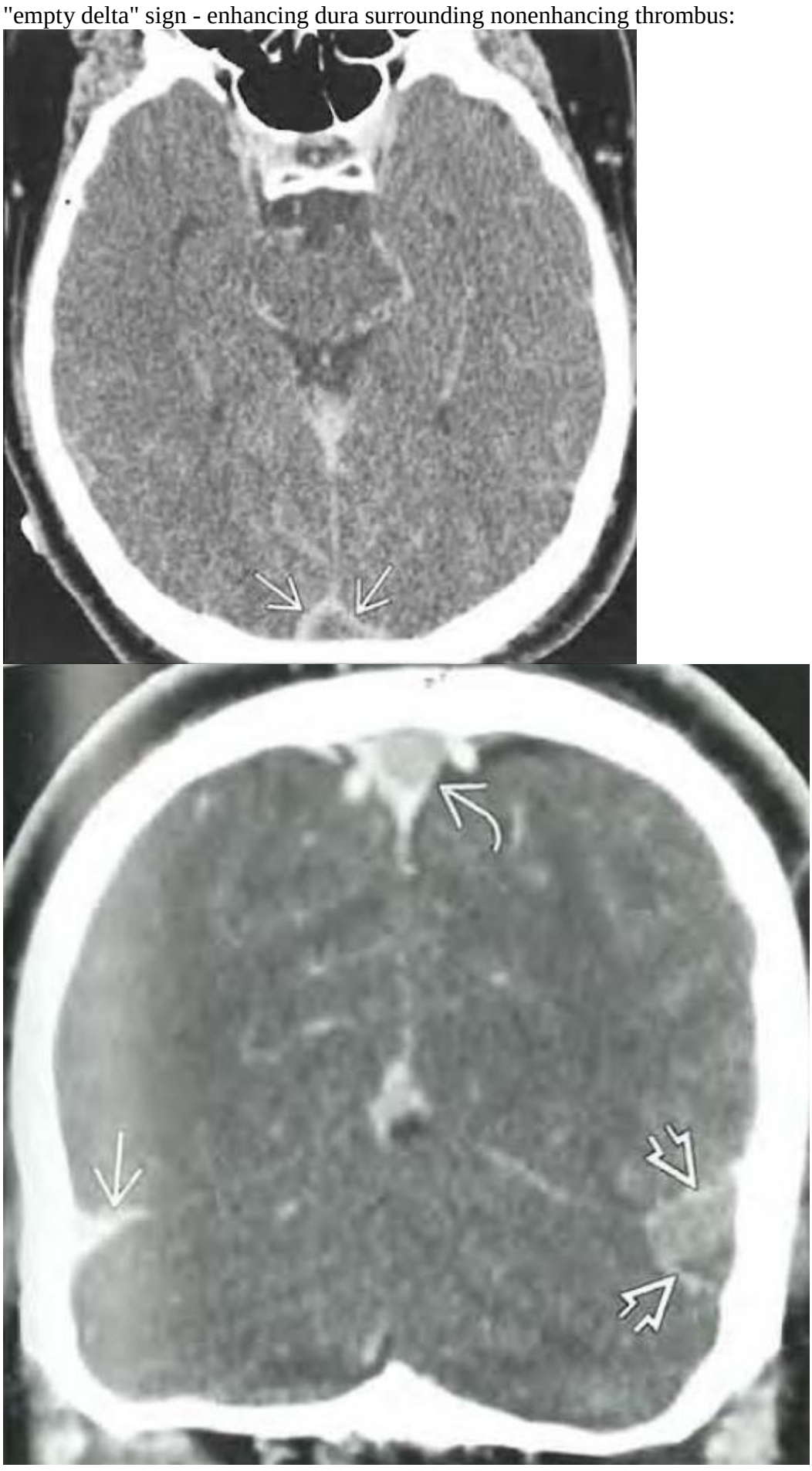
- useful in ***ruling out other conditions*** – neoplasm, subdural empyema, sinusitis.
- demonstration of infarct may be delayed up to 48-72 hours.
- hemorrhagic infarction:
  parasagittally located - SUPERIOR SAGITTAL SINUS;
  centrally located - STRAIGHT SINUS;
  temporal located - TRANSVERSE and SIGMOID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



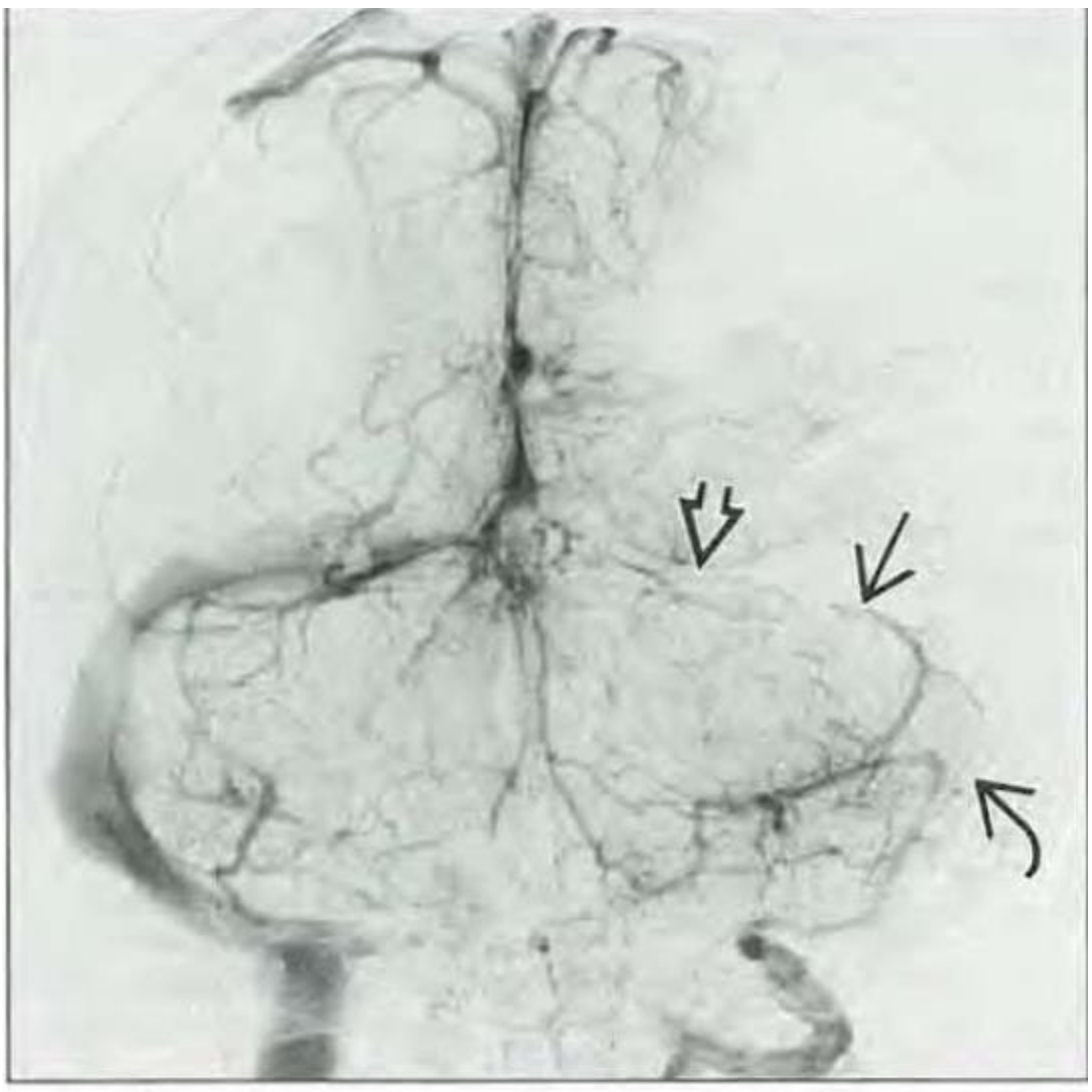
CTV

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

ARTERIOGRAPHY

- 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 absence within dural sinus.
- delayed emptying of cortical veins appear as if they are "***hanging in space***".
- narrowing of intracavernous ICA in CAVERNOUS SINUS thrombosis.
- **direct venography** - passing catheter from jugular vein into TRANSVERSE SINUS.
- **orbital venography** is most definitive method for CAVERNOUS SINUS thrombosis.



9-24. AP view, venous phase, of vertebrobasilar DSA in a patient with occlusion of the left TS and sigmoid sinus. Note clot in adjacent tentorial vein.

EEG

- normal ÷ 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 - leukocytosis (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 ≈ 97.1%, negative predictive value ≈ 99.6%, specificity ≈ 91.2%, positive predictive value ≈ 55.7%.

Hypercoagulable workup:

1) antithrombin
2) protein C, protein S
3) factor V Leiden
4) prothrombin gene G20210A mutation
5) lupus anticoag
6) anticardiolipin antibodies
7) anti beta2 glycoprotein-1 antibodies
8) sickle cell preparation / Hb electrophoresis (individuals of African decent), ESR & antinuclear antibody, liver function tests (cirrhosis).

- tests for hypercoagulable states should not be made while patient is on anticoagulants.

URINE

- nephrotic syndrome.

DIFFERENTIAL

1) hypoplastic or absent sinus segment
2) giant arachnoid granulation

TREATMENT

MEDICAL

1. **ANTICOAGULATION** in therapeutic doses ASAP (HEPARIN → WARFARIN INR goal of 2-3) even if hemorrhagic infarction is present!!!!!!
   - **LMWH** may be preferable to unfractionated heparin.
   - duration: for ***unprovoked*** thromboses - 6-12 months → reimage and decide for continued anticoagulation; if patient is ***prothrombotic***, duration is indefinite
   - may be followed with ASPIRIN.

2. **ANTIBIOTICS** for *septic thrombosis* (empirically start with antistaphylococcal a/b).
   for CAVERNOUS SINUS thrombosis - NAFCILLIN OR VANCOMYCIN + METRONIDAZOLE + 3rd-generation cephalosporin.

3. **Supportive treatment** similar to arterial stroke (esp. reducing ICP, anticonvulsants).

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.

SURGICAL

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

*e.g. comatose with papilledema

- 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.

BIBLIOGRAPHY for ch. "Neurovascular Disorders" → follow this LINK >>