Cerebral Vein and Dural Sinus Venous Thrombosis

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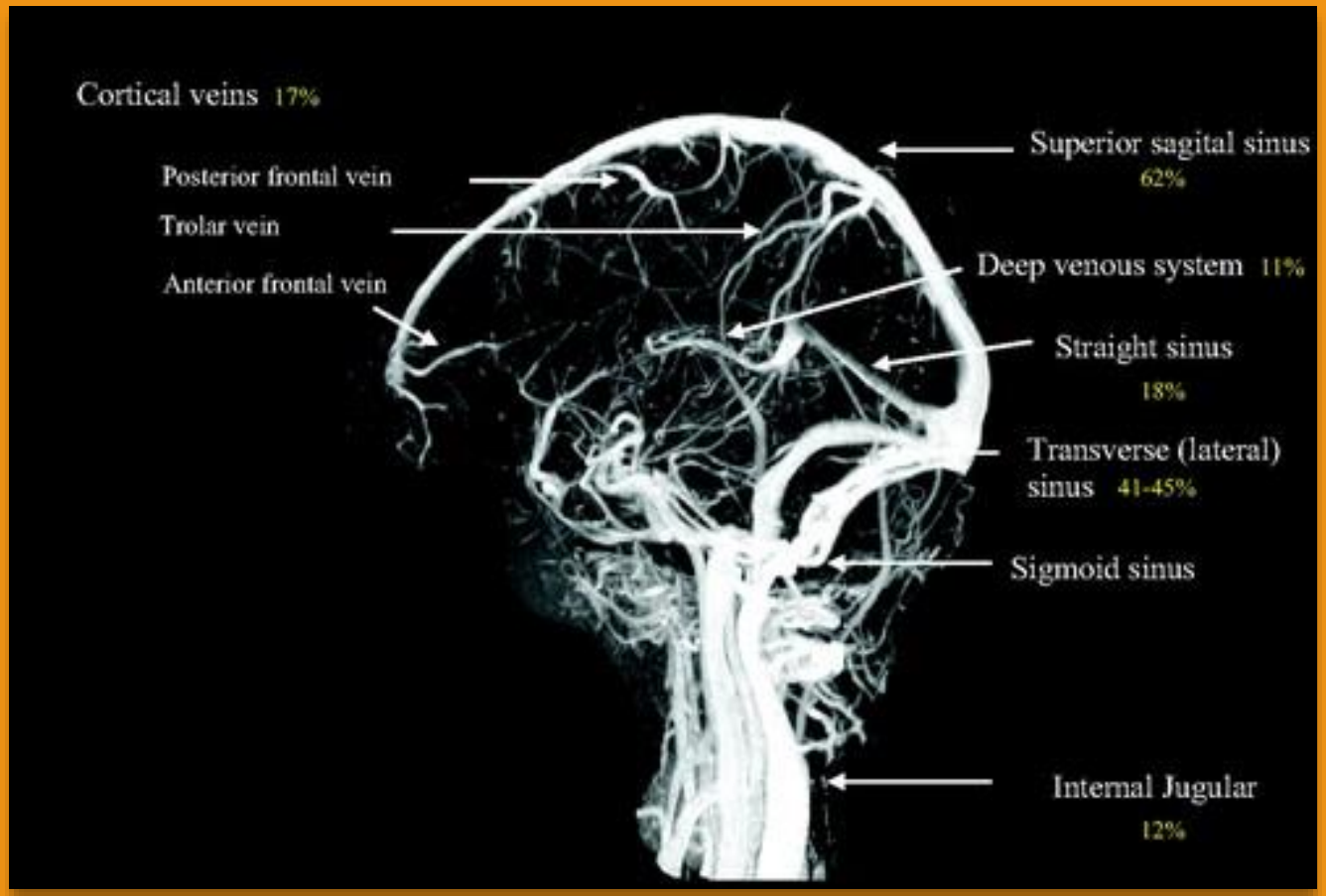
Definition

- Cerebral vein thrombosis (CVT)
  - Thrombosis of the cerebral veins, which tend to be small
    - Cerebral veins are divided into the external (ex. Cortical veins) and internal cerebral veins
- Dural sinus venous thrombosis
  - Thrombosis of the dural venous sinuses, which tend to be large
    - Venous sinuses receive blood from the cerebral veins and cerebrospinal fluid (CSF) from the subarachnoid space
- Essentially, they are venous strokes



Background information

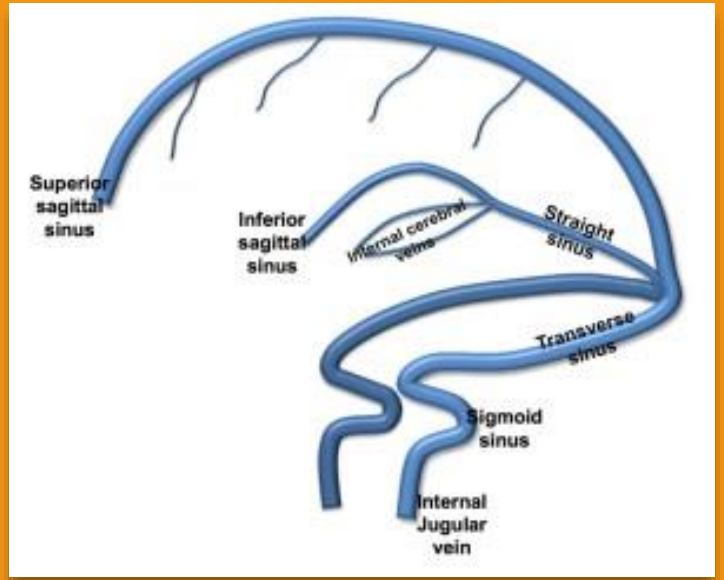
- Epidemiology
  - Uncommon (venous-to-arterial stroke ratio 1:62.5)
    - Annual incidence 1.16 to 2.02 per 100,000
  - More common in females (female-to-male ratio 3:1)
    - May be due to pregnancy or use of oral contraceptive pills (OCP)
  - Tends to affect younger patients compared to arterial strokes (median age 37 years old)
- Pathophysiology
  - Cerebral venous obstruction → ↑ venous / capillary pressure → blood-brain barrier disruption → vasogenic edema
    - Continued ↑ venous pressure → venous hemorrhage vs ↓ cerebral blood flow (which can result in venous infarction)
  - Thrombosed dural sinuses → impaired CSF absorption → ↑ intracranial pressure (ICP) → possible herniation
- Risk factors
  - Most common acquired risk factors are pregnancy, OCP usage, and obesity
  - Most common risk factors for those >65 years old are thrombophilia (genetic or acquired), malignancy, and hematologic disorders (ex. Polycythemia)
    - Genetic thrombophilias include:
      - Antithrombin deficiency
      - Protein C and S deficiency
      - Factor V Leiden pathologic variant
      - Hyperhomocysteinemia
  - Infection (6-12% of cases)
  - Head injury / mechanical precipitants (ex. jugular catheter placement)
  - Inflammatory disorders (systemic lupus erythematosus [SLE], Wegener granulomatosis, temporal arteritis, Behcet disease)

Presentation

- 3 different type of presentations are common:
  - Intracranial hypertension syndrome
    - Headache (most frequent symptom), +/- vomiting, papilledema, visual problems
      - Headache (can be focal or diffuse) usually worsens with Valsalva maneuver or lying down
  - Focal syndrome
    - Focal deficits, seizure
      - Seizures (focal or generalized) are more common in CVT than in other cerebrovascular disorders
  - Encephalopathy
    - Multi-focal neurologic deficits, mental status changes (including stupor or coma)
      - Can be found in severe cases of CVT

Presentation

- Focal syndromes can vary, depending on location of thrombosis
  - CVT's
    - Cortical vein thrombosis
      - Motor/sensory deficits, seizures
  - Sinus venous thromboses
    - Cavernous sinus thrombosis
      - Ocular s/s (orbital pain, chemosis, proptosis, oculomotor palsy)
    - Sagittal sinus thrombosis
      - Motor deficits (often bilateral), seizures
    - Lateral sinus thrombosis
      - Intracranial hypertension (including headache)
      - Aphasia if left transverse sinus is occluded
  - Thrombosis of deep cerebral veins (Ex. Straight sinus, internal cerebral veins)
    - S/s are often severe; can include altered mental status, motor deficits (often bilateral), and coma

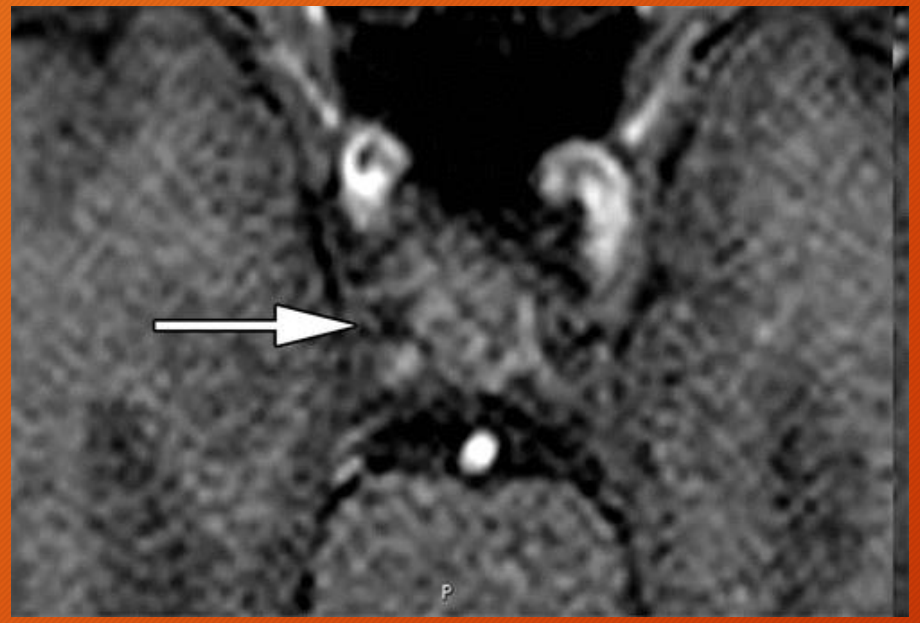


Diagnosis – obtain urgent imaging

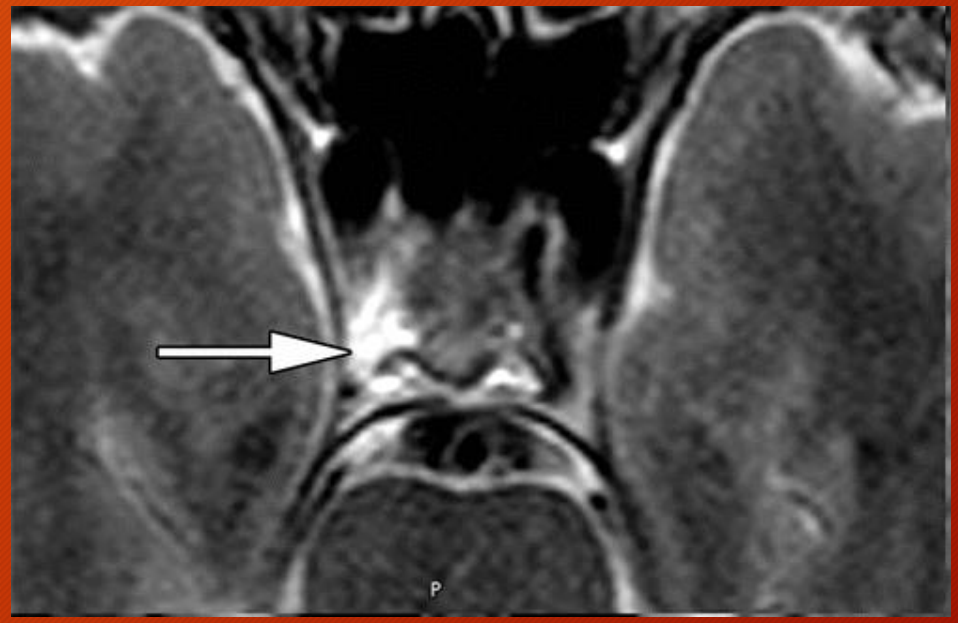
- MRI brain with venography
  - Most sensitive imaging method
  - Within the 1st 5 days:
    - Thrombus appears isointense on T1-weighted images and hypointense on T2-weighted images
  - >5 days:
    - Thrombus more apparent due to ↑ signal on T1 and T2 weighted images
  - >1 month:
    - Signal pattern is more variable and thrombus may appear isointense
  - Parenchymal brain lesions (vasogenic edema, venous infarction) can present as:
    - Hypointense / isointense on T1 weighted images
    - Hyperintense on T2 weighted images
- CT brain with venography (if MRI unavailable or delayed)
  - Is quicker and more readily available than MRI
  - Non-contrast CT brain is normal in ~30% of CVT cases and most CVT findings are non-specific
    - ~1/3rd of cases will show direct signs of CVT ("cord sign", "dense clot sign")
  - Accuracy of non-contrast CT brain + venography is 90-100%
    - On venography, the contrast can enhance a triangular filling defect within the straight sagittal sinus called the "empty delta sign"
  - However, provides limited resolution of the deep venous system
- Conventional angiogram (if CT or MRI inconclusive)
  - Performed via digital subtraction angiography (DSA)

MRI findings

Right cavernous sinus thrombosis, T1 weighted, hypointense signal

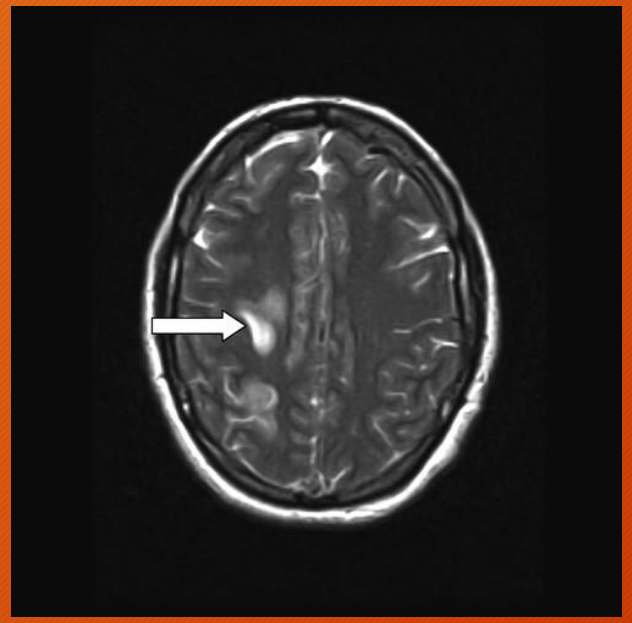


Right cavernous sinus thrombosis, T2 weighted, hyperintense signal

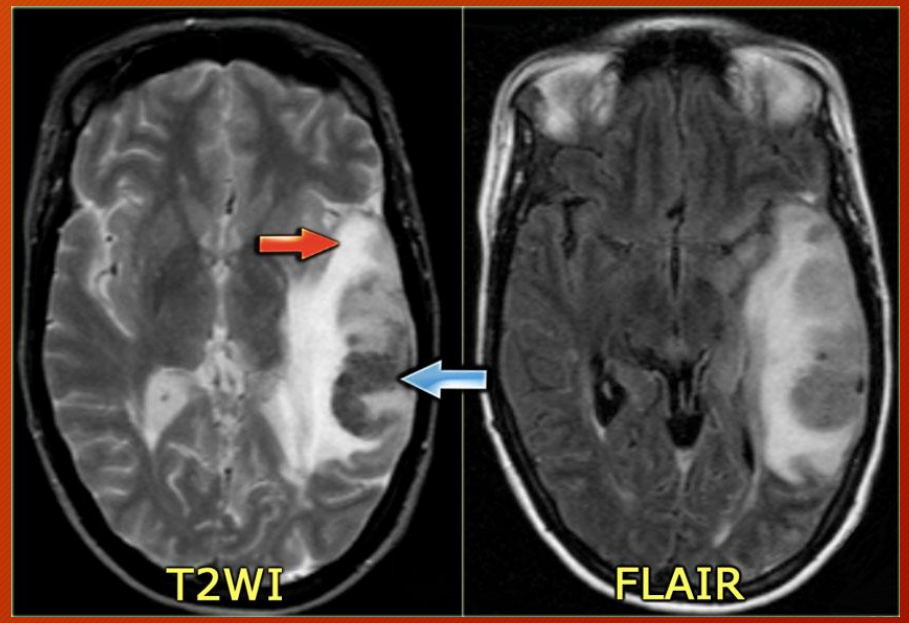


MRI findings – parenchymal lesions

Right frontal lobe venous infarct, T2 weighted, hyperintense signal

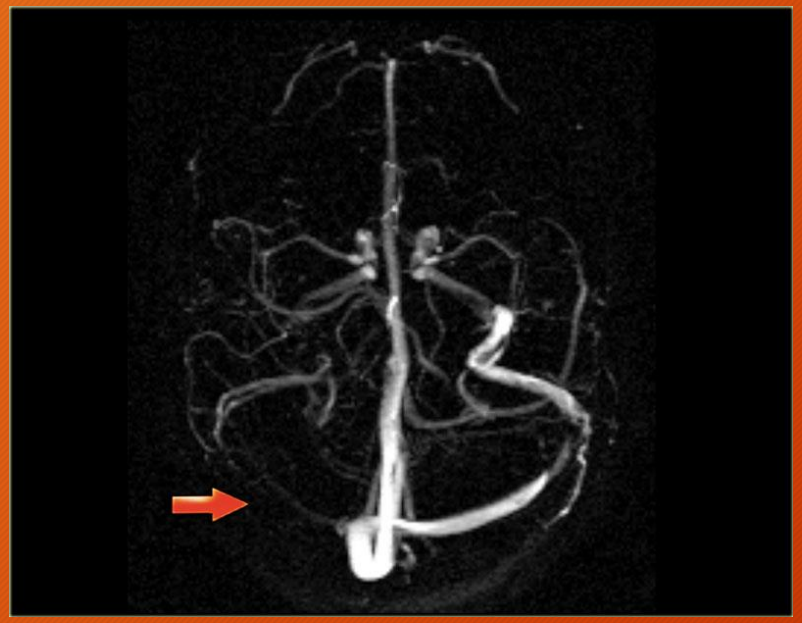


Likely thrombosis of left vein of Labbe, vasogenic edema (red arrow), intracerebral hemorrhage [ICH] (blue arrow)

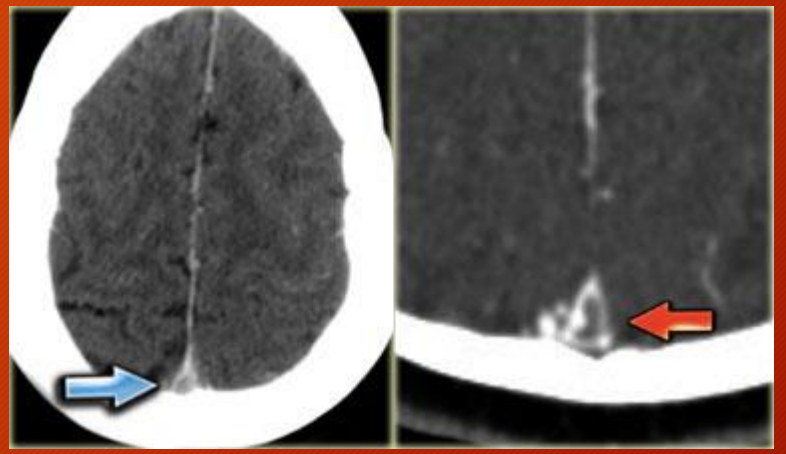


MRI and CT venography

Right transverse sinus and internal jugular vein thrombosis, filling defect in MRI venography (red arrow)

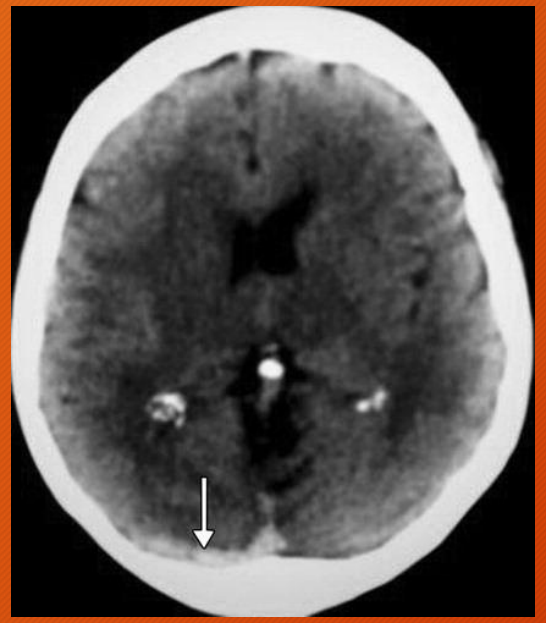


Superior sagittal sinus thrombosis, “empty delta sign” in CT venography

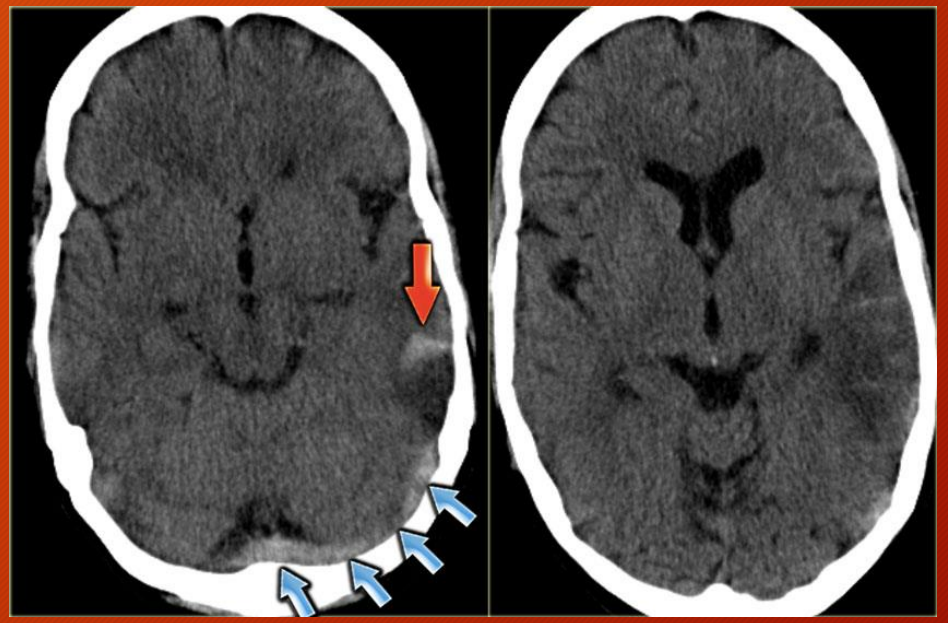


Non-contrast CT findings

“Cord sign”

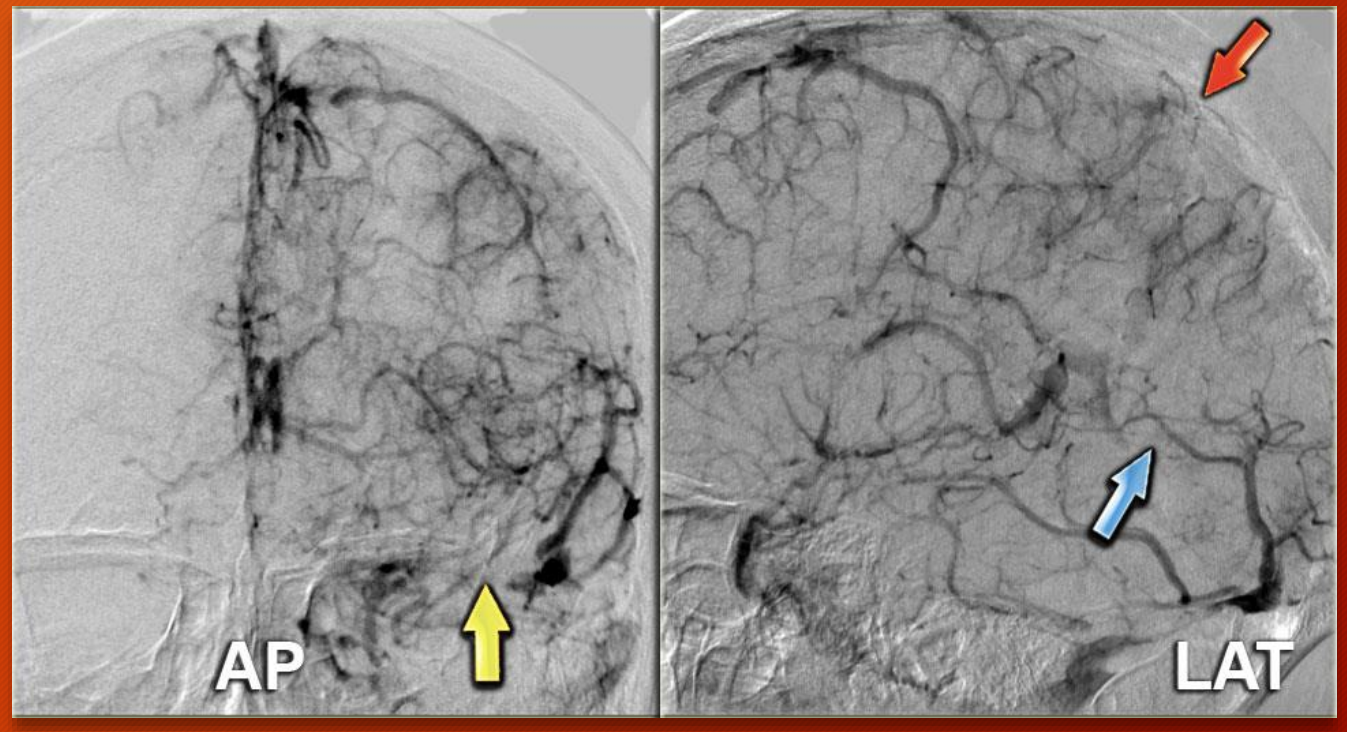


“Dense clot sign”



Conventional angiogram (or DSA) findings

- Yellow arrow – thrombosis of transverse and sigmoid sinus
- Red arrow – thrombosis of superior sagittal sinus
- Blue arrow – thrombosis of straight sinus



Laboratory workup

Routine blood studies

- AHA/ASA guidelines recommend the following for suspected CVT patients:
  - Complete blood count (CBC)
  - Chemistry panel
  - Prothrombin time (PT)
  - Activated partial thromboplastin time (aPTT)
- D-dimer
  - Elevated plasma level supports CVT, though a normal level does not exclude it
  - Sensitivity (84-92%), specificity (83-98%)
- Lumbar puncture
  - Helpful to r/o meningitis as possible affiliated infectious process in CVT
  - Can also be valuable to measure and decrease CSF pressure when vision is threatened
  - Overall, in the absence of suspicion for meningitis, CSF analysis is not helpful diagnostically when compared to neuroimaging

Testing for prothrombotic conditions

- Protein C, Protein S, antithrombin deficiency
  - This is generally indicated 2-4 weeks after completion of anticoagulation, not in acute setting or while patient is taking Warfarin
- Antiphospholipid syndrome
- Prothrombin G20210A
- Factor V Leiden
- Homocysteine
- Erythrocyte sedimentation rate (ESR) and antinuclear antibody (ANA) studies to r/o SLE, Wegener granulomatosis, and temporal arteritis
- Sickle cell preparation or hemoglobin electrophoresis should be considered for patients of African descent
- Urine protein to r/o nephrotic syndrome
- Liver function tests (LFT's) to r/o cirrhosis

Acute management

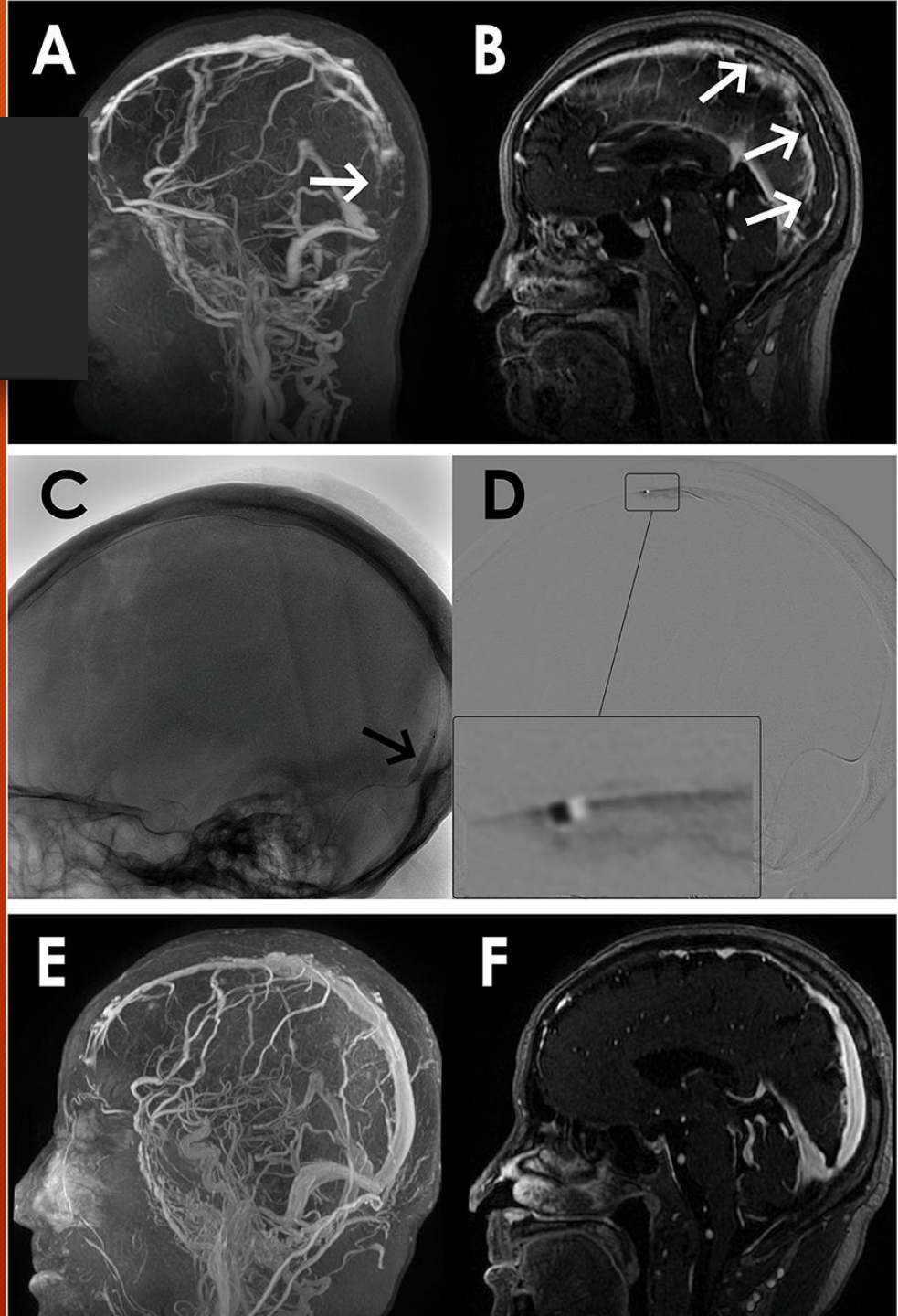
- Anticoagulation is the mainstay of acute / subacute treatment
  - Purpose is to recanalize the occluded vein, avoid thrombus propagation, and treat the underlying prothrombotic state
  - Therapeutic dose subcutaneous low molecular weight heparin (ex. Enoxaparin) vs IV heparin are typically recommended for adults with symptomatic CVT without contraindication
    - alternatives (ex. Argatroban) can be considered in certain situations like heparin-induced thrombocytopenia (HIT)
  - Presence of bleed (hemorrhagic venous infarct, ICH, subarachnoid hemorrhage [SAH]) is not a contraindication for anticoagulation
    - Some studies showed that none of the patients who were randomized to heparin treatment developed a new ICH
      - It is speculated that hemorrhage in CVT is likely due to venous outflow occlusion → elevated venous pressure → venule rupture + hemorrhagic transformation of venous infarcts
  - Per ASA guidelines:
    - “In conclusion, limited data from randomized controlled clinical trials in combination with observational data on outcomes and bleeding complications of anticoagulation support a role for anticoagulation in treatment of CVT, regardless of the presence of pretreatment ICH.”

Endovascular options for acute management

- Direct catheter thrombolysis vs direct mechanical thrombectomy +/- thrombolysis
  - There are no randomized trials supporting these interventions in comparison to anticoagulation therapy
  - However, it should be noted that ~9-13% of patients with CVT have poor outcomes despite anticoagulation
    - Some studies showed 82.5% partial or complete recanalization with just anticoagulation at 3-6 months
  - Endovascular interventions may be worth considering if there is continued clinical deterioration despite anticoagulation
- Direct catheter thrombolysis
  - Thrombolytic agent is delivered after a microcatheter and microguidewire are deployed to the thrombosed sinus via a sheath or guiding catheter at the jugular bulb
  - 1 limited study showed recanalization in 96% of patients
  - However, 1 review showed that ICH occurred in 17% of patients after thrombolysis and was affiliated with clinical worsening in ~5%.
- Mechanical thrombectomy
  - Balloon-assisted thrombectomy
    - Balloon can be used to perform partial thrombectomy prior to thrombolysis
  - Catheter thrombectomy
    - Rheolytic catheter thrombectomy
      - Thrombolysis is performed via high-velocity saline jets
        - Disrupted thrombus is then aspirated into a 2nd lumen of the device
    - Thrombectomy via thrombus-retrieval device
      - Device may perform partial recanalization, which can be followed up with thrombolysis
    - Thrombectomy via device that debulks and aspirates acute thrombi

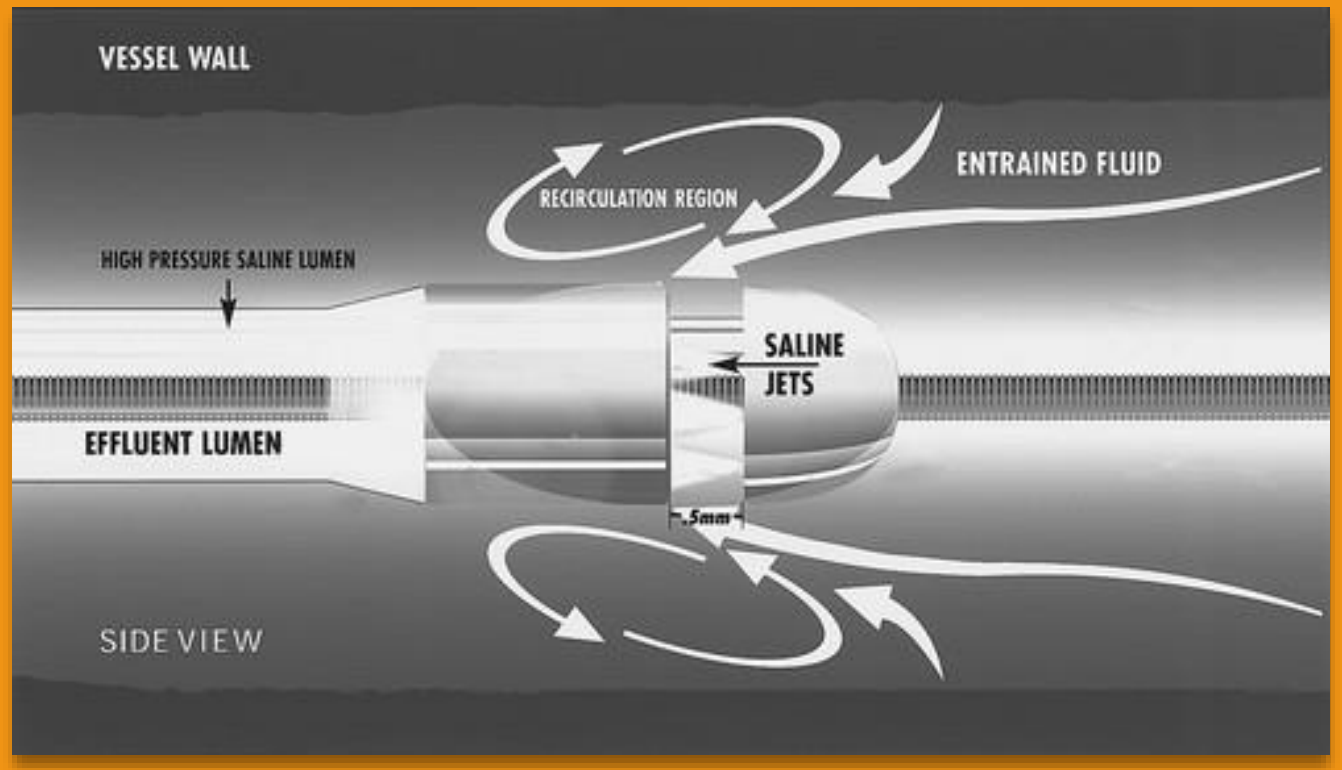
Balloon-assisted thrombectomy

- A and B:
  - superior sagittal sinus thrombosis
- C:
  - balloon dilatation (black arrow) of superior sagittal sinus
- D:
  - retained microcatheter at superior sagittal sinus to continuously inject thrombolytic agent (urokinase)
- E and F:
  - Recanalization of superior sagittal sinus



Rheolytic catheter thrombectomy

1. High-pressure saline jets → low-pressure zone and vortices around the catheter tip → thrombus is disrupted
2. Disrupted thrombus is aspirated into the effluent lumen of the catheter



Other issues for acute management

- Elevated ICP – follow standard measures for acute ICP control
  - Elevate head of bed by 30-45 degrees
  - ICU admission
  - Mild sedation as needed
  - Osmotic therapy (mannitol vs hypertonic saline)
  - Temporary hyperventilation to target $PaCO_2$ 30-35mm Hg
  - Consider ICP monitoring
  - There's no evidence to support usage of glucocorticoids (Ex. Dexamethasone) in the absence of an underlying inflammatory disorder provoking the CVT
- Impending brain herniation (due to unilateral hemispheric lesion)
  - Hemicraniectomy can be a lifesaving intervention (consult Neurosurgery)
- Seizure
  - Seizure prophylaxis is recommended only for patients with both seizure at presentation and supratentorial lesion (vasogenic edema, venous infarct, ICH) on neuroimaging
    - Prophylaxis is not necessarily required for an isolated early symptomatic seizure when there is no supratentorial lesion, as there is often no seizure recurrence
    - Prophylaxis is not recommended for patients with cerebral lesions without seizure
- Treat underlying infection or inflammatory disorder
  - Particularly treat, if present, meningitis or infection of neighboring structure (otitis, mastoiditis)
  - Treat associated inflammatory disorder (ex. SLE) with glucocorticoids if necessary

Prognosis in the acute phase

- ~5% of patients die in the acute phase of CVT
  - Main cause is transtentorial herniation due to large hemorrhagic lesion
  - Other causes include:
    - Herniation due to multiple lesions vs diffuse cerebral edema
    - Status epilepticus
    - Pulmonary embolism
    - Medical complications
- Predictors of mortality within 30 days were noted as follows:
  - Depressed consciousness
  - Altered mental status
  - Thrombosis of the deep venous system (ex. Straight sinus)
  - Right hemisphere hemorrhage
  - Posterior fossa lesions

Prognosis in the long-term

- Death or dependency rate on follow up (ranging 3-78 months) is ~15%
- Predictors of poor long-term prognosis:
  - Central nervous system (CNS) infection
  - Malignancy
  - Thrombosis of the deep venous system
  - Intracranial hemorrhage
  - Glasgow coma scale <9 on admit
  - Altered mental status
  - Age >37 years old
  - Male sex

- CVT risk score can help estimate functional prognosis at 6 months post-CVT onset

Prognostic variable	Risk points
Malignancy	2
Coma	2
Thrombosis of deep cerebral veins	2
Mental status disturbance	1
Male sex	1
Intracranial hemorrhage	1
	Total risk points • <3: Low risk of poor outcome ≥3: High risk of poor outcome

References

- Images:
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