18 y.o. man with R leg pain

Dr. Julie Henseler
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History

- **PMH:** seizure 2003 (fell and hit head); allergic rhinitis
- **Meds:** allegra, singulair
- **Allergies:** PCN
- **Social:** senior in high school; no bad habits; lives with parents; enjoys contact sports
- **Family history:** father - HTN
HPI

- Developed R leg pain with activity; played football throughout summer; no h/o trauma
- Throbbing pain involving posterior R knee and leg; worse with flexion and extension of ankle
- Presented to PMD: mild erythema and tenderness of the R leg
HPI - continued

- PMD visit:
  - D-dimer positive
  - US positive for DVT
  - Heterozygous for F-r V Leiden
  - Lovenox; transitioned to Coumadin
  - 6 week f/u: pain and swelling resolved; requested clearance to play football
3 weeks later

- Headache behind L eye
- Low grade fever
- Nausea, vomiting x 2 days
- Photophobia
- Presented to OSH ED
- No flow in left transverse sinus consistent with sinus thrombosis
- MR brain otherwise normal
Cerebral Venous Thrombosis

- Incidence in patients < 18 yo: 67 per 100,000 per year (multi-center Canadian registry)
- More common in women: 2.9:1 (OCP, pregnancy)
- CVT in pregnancy: 11.6 per 100,000 deliveries (US hospital discharge registry)
- Mean age 39, only 8% > 65 yo

Source: Ferro, Jose et al “Etiology, Clinical Features, and Diagnosis of Cerebral Venous Thrombosis”. UpToDate v15.3.2008
Venous blood from the brain flows from the cortical & deep cerebral veins into the venous (dural) sinuses.

Source: Ferro, Jose et al. “Etiology, Clinical Features, and Diagnosis of Cerebral Venous Thrombosis”. Up To Date v15.3:2008
Risk Factors

- Prothrombotic conditions: F-r V Leiden, Prot C, Prot S, ATIII, Prothrombin mutation, antiphospholipid antibody, nephrotic syndrome
- OCPs; Pregnancy and postpartum period
- Local infection (otitis, sinusitis); sepsis; dehydration
- Head trauma; LP
- Malignancy; invasion by adjacent tumor
Mechanisms of CVT

CSF absorption occurs in the arachnoid granulations, which drain CSF into the superior sagittal sinus.
Major Clinical Syndromes

- Isolated intracranial hypertension (headache, +/- vomiting, papilledema, visual problems)
- Focal syndrome (motor weakness, hemiparesis, aphasia, seizures)
- Encephalopathy (mental status changes, stupor, coma, multifocal signs)
- Headache: severe, dull, generalized pain that worsens with Valsalva and with recumbency.
Clinical Features

- Cavernous sinus: orbital pain, chemosis, proptosis, oculomotor palsy
- Sagittal sinus: motor deficits, bilateral deficits, seizures
- Lateral sinus: isolated intracranial hypertension
- Jugular vein or lateral sinus: tinnitus; cranial nerve pulsies
Diagnosis of CVT

- Abnormal signal in a venous sinus on MRI in combination with the corresponding absence of flow on MR venography confirms the diagnosis.
- Head CT: normal in 30% of CVT cases
- Cerebral angiography when the diagnosis is uncertain
- Imaging may reveal parenchymal lesions: brain edema or venous infarction
- Search for a thrombophilic state
Factor V Leiden

- Most common cause of inherited thrombophilia (40 – 50% of cases)
- F-r Va serves as a cofactor in the conversion of prothrombin to thrombin
- F-r Va is inactivated by protein C
- Replacement of arginine by glutamine at position 506 in F-r V due to gene mutation results into F-r V Leiden
F-r V Leiden

- Not susceptible to cleavage at position 506 by activated protein C → inactivated more slowly
- More f-r V is available → increased generation of thrombin
- Slower degradation of f-r VIIIa due to deficiency of f-r V cleavage product
## Risks of a first episode of venous thrombosis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>1</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>2.5</td>
</tr>
<tr>
<td>Prothrombin gene mutation</td>
<td>2.8</td>
</tr>
<tr>
<td>OCP</td>
<td>4</td>
</tr>
<tr>
<td>F-r V Leiden (heterozygous)</td>
<td>7</td>
</tr>
<tr>
<td>OCP + heterozygous F-r V Leiden</td>
<td>35</td>
</tr>
<tr>
<td>F-r V Leiden (homozygous)</td>
<td>80</td>
</tr>
</tbody>
</table>

Data from the Leiden Thrombophilia Study
CT scan demonstrates a subtle right transverse sinus thrombosis with high attenuation (arrows)
A noncontrast CT image located above Image 1 demonstrates thrombus (arrows) extending along the course of the right transverse sinus.
MR venography demonstrates absent flow in the right transverse sinus, sigmoid sinus, and internal jugular vein.
A 32-year-old postpartum patient with headaches. Axial CT image shows a hypodense left temporal lobe venous infarct. A triangular high-attenuation focus (arrows) posterolateral to the area of infarction represents thrombus within the left transverse sinus.
Sagittal T1-weighted image demonstrates T1-hyperintense thrombus (arrows) within the superior sagittal sinus consistent with thrombus.