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An Atypical Presentation of Cerebral Venous Sinus Thrombosis in a 19-Year-Old Woman

AUTHORS:
Mercedes Malone, MD[1] • David Ritchie, MD[2] • Peters Okonoboh, MD[1] • Ahmed Ebrahim, MD[1]

AFFILIATIONS:
[1]College of Medicine, University of Central Florida, Orlando, FL; Internal Medicine Residency Program, HCA Florida North Florida Hospital, Gainesville, FL
[2]General Surgery Residency Program, HCA Florida Kendall Regional, Miami, FL

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CORRESPONDENCE:
Mercedes Malone, MD, University of Central Florida College of Medicine, Graduate Medical Education, 6850 Lake Nona Boulevard, Orlando, FL 32827 (doctormercedesmalone@gmail.com)

A 19-year-old woman presented to the hospital after she was discovered to be unresponsive by her family.

History. The patient had a medical history of anxiety, depression, untreated pediculosis capitis of 1-year duration, and bulimia-purge-type disorder. Her psychiatric history included anxiety episodes of dermatillomania and stereotypic movement disorders, such as head-banging. She was last evaluated by a medical professional a year prior but was lost to follow-up and not receiving any treatments for her conditions. She had previously been in normal health except

for a few days of increased anxiety and episodes of head-banging. The patient's family denied any associated recent traumatic event. There was no history of substance abuse or tobacco use. There was also no history of hypercoagulable disorders, brain aneurysms, or autoimmune conditions in her or her family.

Upon arrival to the hospital, the patient exhibited generalized seizure-like activity consistent with status epilepticus. Physical examination revealed no visible signs of trauma. Her Glasgow Coma Scale score was 6, with 1 point scored for best verbal response, 1 for best eye response, and 4 for best motor response. Musculoskeletal examination was within normal limits for muscle tone in bilateral upper and lower extremities. Deep tendon reflexes were intact and adequately evoked at the biceps and knees bilaterally. All other aspects of her physical examination were unremarkable, including cardiopulmonary and abdominal examination.

She was intubated for airway protection due to persistent loss of consciousness and concern for inability to protect her airway. Antiepileptic medications and subsequent antiseizure prophylactic medications were administered.

Diagnostic testing. Laboratory workup was remarkable for severe microcytic anemia with a hemoglobin level of 4.8 g/dL. The patient required multiple blood transfusions to increase her hemoglobin level above 7 g/dL. A pelvic ultrasound revealed an endometrium that measured 12.3 mm in thickness. The findings correlated the anemia to her menstrual cycle. A urine toxicology screening was negative.

An initial computerized tomography (CT) scan of her brain without contrast showed a combination of subarachnoid hemorrhage as well as bilateral cortical petechial hemorrhages (Figure 1). After approximately 5 hours, a magnetic resonance venography (MRV) was performed due to high clinical suspicion and the patient's age. The MRV showed a filling defect within the anterior portion of her superior sagittal sinus, indicating a thrombus (Figure 2). The MRV findings led to an ultimate diagnosis of cerebral venous sinus thrombosis (CVST) and an angiogram was ordered.

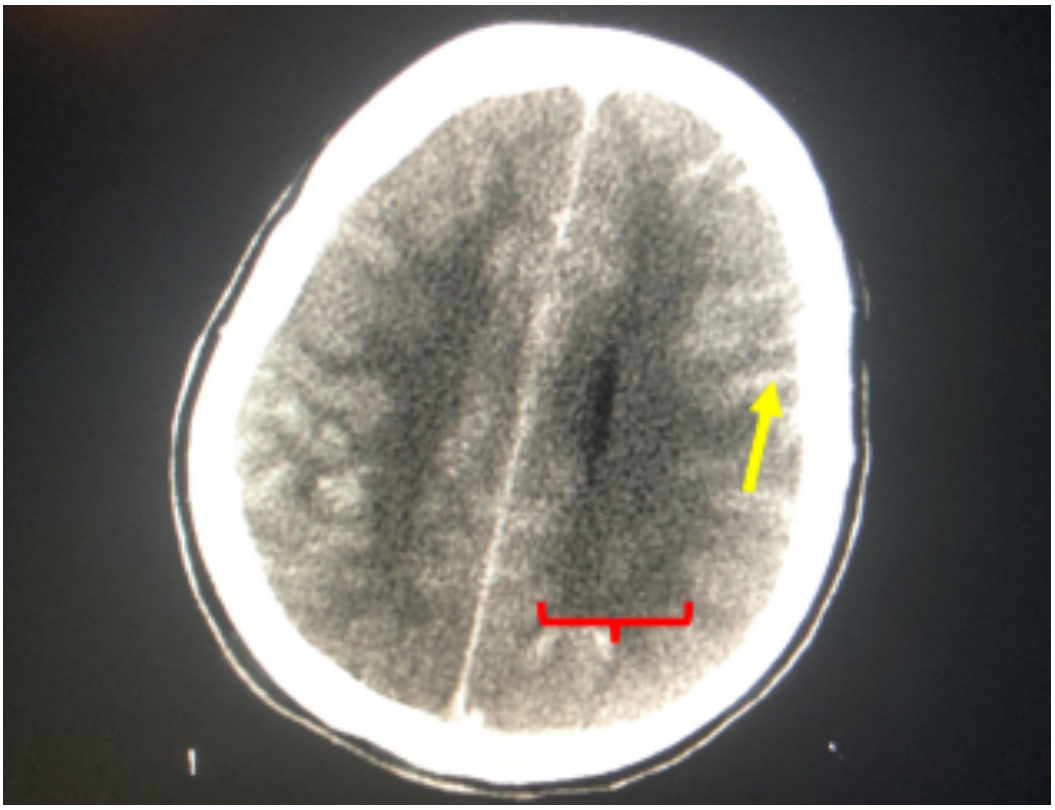

Figure 1. *Brain CT without contrast shows the area of subarachnoid blood (arrow) and an area of noticeable cortical and white matter edema (bracket).*

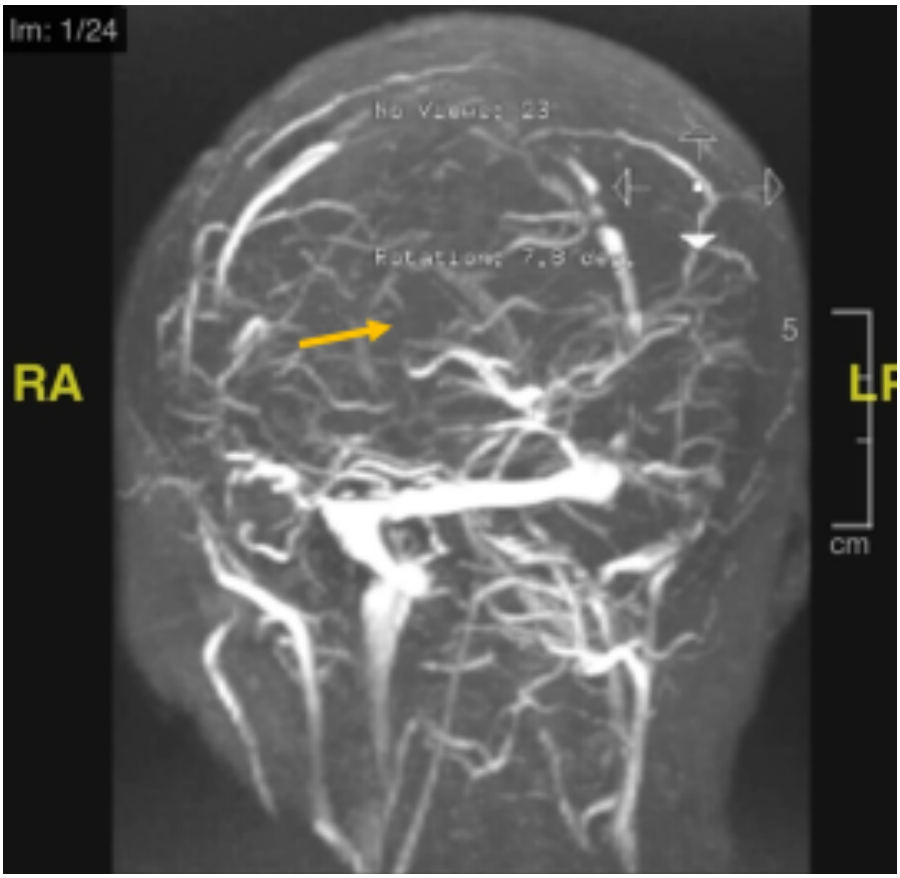

Figure 2. *Magnetic resonance venography shows the filling defect within the superior sagittal sinus (arrow), suggesting thrombosis.*

Differential diagnoses. Substance overdose, meningitis, and trauma can mimic the presentation of CVST and are in the differential diagnosis.

Our patient presented with the second most common finding of generalized seizure. Despite this, her diagnosis of CVST was initially obscured by the atypical radiologic finding of subarachnoid hemorrhage. This finding suggested that possible traumatic brain injury or substance use was the likely cause of her symptoms. However, the patient lacked visible signs of trauma, and her cerebral imaging did not illustrate brain contusion or coup or contra-coup signs. Her history of head-banging could have contributed to the formation of cranial hemorrhage, but this may have distracted from the underlying CVST diagnosis. The lack of substance abuse history and negative urine test also led us to a diagnosis of CVST. Additionally, the absence of infection signs (such as fever), specific MRV findings showing a thrombus in the superior sagittal sinus, and the patient's clinical history favored CVST over meningitis as the correct diagnosis.

Treatment and management. The patient underwent mechanical thrombectomy to open her occluded superior sagittal sinus (Figure 3). Recanalization was achieved after thrombectomy.

She was monitored in the critical care unit with close neurologic testing. A repeat brain MRI performed immediately after and a few days later showed no new thrombosis and remained stable. A continuous heparin drip was started with the goal of heparin anti-factor Xa range between 0.3 and 0.5 IU/mL. Serial daily brain CT imaging was stable without any acute or significant findings.

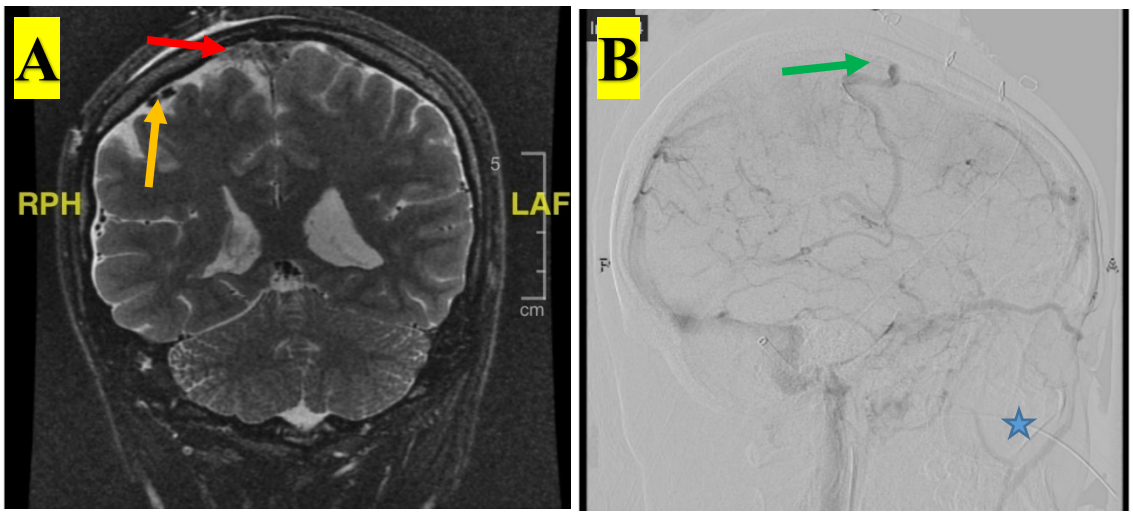

Figure 3. *Cerebral angiogram shows (A) the filling defect seen in the superior sagittal sinus (red arrow) and the normal area of what is expected to be seen in comparison with the thrombosis (yellow arrow), and (B) the area of filling defect (green arrow) and the area where a segment of the thrombectomy wire can be visualized (blue star).*

Outcome and follow-up. While her neurologic status improved during 3 weeks of monitoring in the hospital, she began displaying behavioral abnormalities, including head-banging movements. Hereditary and genetic causes of thrombophilia were to be assessed in the outpatient setting, and her oral contraceptives were discontinued indefinitely. She was discharged from the hospital in stable condition with instructions to take apixaban 10 mg twice daily for 7 days, then 5 mg twice daily, and an outpatient follow-up scheduled with a hematologist.

Discussion. CVST is a rare entity. One study estimates the yearly incident rate to be roughly 3 to 4 cases per 1 million people, or roughly 0.0003% in adults. The incident rate is slightly higher in children, at 7 cases per 1 million.[1] Most cases have been noted in young women (mean age of 35 years) who are taking oral contraceptive pills.[1,2]

CVST occurs when there is a clot in the vasculature system responsible for draining the venous blood supply of the brain. The lodged clot leads to alterations in the venous capillary pressure, disruptions in the blood brain barrier, and ultimately results in vasogenic edema and venous hemorrhage.[3]

There are various risk factors for the development of a thrombosis in the cerebral venous vasculature. Most risk factors are associated with conditions that lead to a hypercoaguable

state. Some risk factors include iron deficiency anemia, oral contraceptive pill consumption, pregnancy, female biological sex, malignancy, obesity, and chronic inflammatory states. In addition, some studies have reported a correlation between CVST and lower levels of hemoglobin; the suggested mechanism was that iron deficiency anemia could lead to thrombocytosis and increase clot formation.[4] Oral contraceptives have been associated with development of CVST,[5,6] likely due to estrogen's prothrombotic properties.

It is imperative to evaluate for both congenital and acquired causes of thrombophilia. Several acquired risk factors increased the case patient's susceptibility to CVST. She had a critically low hemoglobin level of 4.8 g/dL upon admission, which was attributed to iron deficiency anemia due to menorrhagia and may have increased her risk for thrombocytosis. She had untreated pediculosis capitis of 1-year duration and used oral estrogen contraceptive pills. She did not have any known congenital thrombophilia, including prothrombin 20210 mutation (factor II mutation), no presence of antiphospholipid antibodies, and no other common autoimmune conditions. However, she will be undergoing further coagulopathy workup in the outpatient setting.

The clinical presentation of CVST is highly variable and nonspecific and depends on which cerebral sinus is affected. The cerebral venous system can be divided into two major components: the cerebral veins and the dural venous sinuses. The superficial cerebral venous system drains blood from the cerebral cortex mainly into the superior sagittal sinus, which in turn drains into the transverse sinuses. The dural venous sinuses drain blood from the cerebral veins and the cerebrospinal fluid from the subarachnoid space, via the arachnoid granulations, which are present particularly in the superior sagittal sinus.[7] The most common cerebral venous sinuses to become thrombosed include the superior sagittal, transverse, and sigmoid sinuses. The superior sagittal and the transverses are the most affected sinuses (60% of patients), followed by the internal jugular and cortical veins (20%). In nearly two thirds of patients, CVST involves more than one sinus.[1]

Initial presentation may include a combination of headache (88.8%), seizures (39.3%), paresis (37.2%), papilledema (28.3%), and mental status changes (22.0%), according to the International Study on Cerebral Venous and Dural Sinus Thrombosis.[1] Signs of increased intracranial pressure may also be present, such as nausea and vomiting, loss of vision, or focal neurologic deficits.[8] Because of the variability in presentation, the diagnosis is often delayed, with a reported median period of 7 days from the onset of clinical manifestations to diagnosis.[9] However, the diagnosis of CVST has increased in past decades because of improvements in neuroradiologic techniques. If CVST is suspected in adults, CT without contrast is the first-line imaging technique; however, MRV is the standard imaging technique for diagnosing CVST.[2]

Initial treatment and management of CVST is therapeutic anticoagulation to prevent clot propagation and allow for recanalization.[1] Concerns regarding the safety of anticoagulation therapy include the increased risk for cerebral hemorrhagic complications. However, a comprehensive meta-analysis that included 14 studies and 1135 cases concluded that anticoagulation is safe and does not lead to increased bleeding even in the presence of pre-

treatment cerebral hemorrhage.[10] Anticoagulation therapy has shown better outcomes compared with non-anticoagulation treatment interventions. [6,10] The use of endovascular thrombolysis remains controversial and is usually reserved for cases that are severe or worsening despite therapeutic anticoagulation.[5]

Severe cases of CVST often present with complications in the acute phase that require specific individualized management. These complications include seizures, intracranial hypertension, hydrocephalus, and transtentorial herniation. In the case of seizures, antiepileptic drugs are indicated to prevent recurrences.[1] Despite the severity with which CVST can present, favorable outcomes have been reported in patients who receive early diagnosis and treatment.[6]

In conclusion, CVST has a highly variable clinical presentation and emergent nature that necessitates a careful history and synthesis of clinical data. A prompt diagnosis will help minimize morbidity and mortality. Although the occurrence of CVST is rare, it remains one of the leading causes of stroke in young adults and should remain in the differential diagnosis of young female patients presenting with atypical stroke.

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