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A 30-Year-Old Female with Headaches of Increasing Frequency

Urgent message: Cerebral venous sinus thrombosis (CVST) occurs when a blood clot forms in the venous sinuses within the brain, preventing drainage of blood. It can cause blood cells to break down and leak into the brain tissues, forming a hemorrhage. This can result in stroke. CVST affects about 5 people in 1 million per year.

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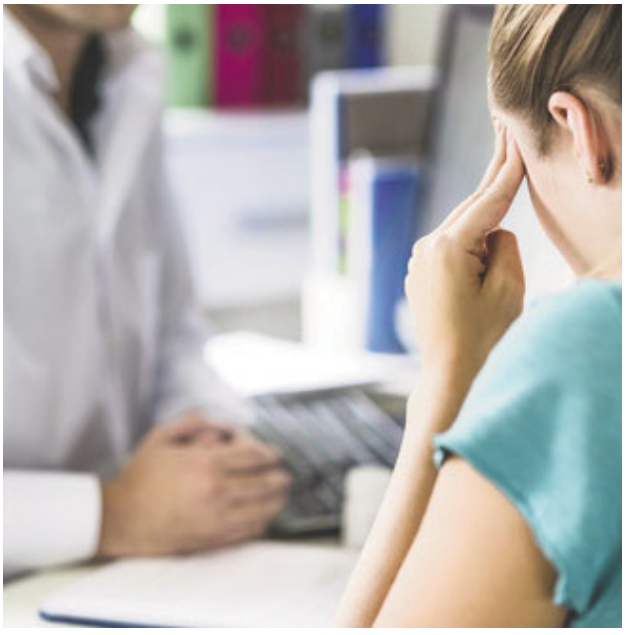
Case Presentation

A 30-year-old female presented to urgent clinic with a headache that had been increasing in frequency over 4 days, often waking her from sleep. She also had retro bulbar pain, along with pulsatile tinnitus. It was associated with nausea but she denied any hemoptysis, weight changes, night sweats, or chills. She denied any past medical history or significant family history. Physical exam revealed a well-nourished, well-developed female who appeared to be in significant distress from occipital and neck pain. She had a benign physical exam, including normal muscle strength and gait. There were no significant cardiopulmonary or gastrointestinal findings. Cranial nerves 3-12 were intact and her gait was normal. Her only medication was a low-dose daily oral contraceptive pill.



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Outcome

At the urgent care, this patient was diagnosed with atypical migraine and was sent home with instructions to follow up with her primary care provider, whom she saw a week later. Her primary care physician ordered magnetic resonance imaging because the patient's symptoms were new in nature, and severe with associated visual changes and nausea. The differential included primary malignancy, pituitary adenoma, pseudotumor cerebri, vertebral artery dissection, and thrombosis. MRI showed extensive thrombosis of the superior sagittal sinus, right transverse, and right sigmoid sinuses with extension into the right internal jugular vein. She was admitted to the hospital for anticoagulation and further management.

The patient was transitioned from unfractionated heparin to enoxaparin (Lovenox) and then eventually bridged to warfarin. The patient's hypercoagulable workup was negative and a computed tomography scan of the chest, abdomen, and pelvis with intravenous and oral contrast done was unremarkable for any signs of malignancy. (CT would not typically be indicated in a

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case like this, but was done at the request of this very anxious patient as a courtesy.) The patient's venous sinus thrombosis was thus thought to be iatrogenically provoked secondary to oral contraceptive use.

Discussion

CVST is a very rare form of venous thromboembolism, representing approximately 0.5%-3% of all types of strokes.[1] Clinical presentation varies from one individual to another and possible clinical manifestations include headache, vision changes, and nausea with vomiting, seizures, stroke, coma, and even death.[2] These symptoms are not all-inclusive—patients may have only one, or may have multiple symptoms.[2,3,]

A minority of patients during presentation have no complaints of headache, which can make diagnosis extremely difficult. Moreover, patients with CVST presenting to an acute care setting are frequently misdiagnosed as having migraine or tension-type headache due to the rarity and possible variation of symptoms at presentation.[4] Although a rare diagnosis, it should be considered in the differential.

"Patients with CVST will often present with headaches, yet the diagnosis can be easily missed due to the rarity of the case and complexity of its presentation. Thus, knowledge of its presentation, risk factors, and common findings are very important in order to avoid delays in diagnosis and avoid life-threatening outcomes."

Risk factors for CVST include pregnancy and puerperium, oral contraceptive use, thrombophilia, malignancy, infections, dehydration, and head traumas. Overall, women are affected more frequently than men.[4,5] Headache is the most common presenting symptom of CVST and is present in about 90% of cases. Based on history, if the patient has signs of elevated intracranial pressure or signs of intracranial hypertension, this can strongly suggest the presence of CVST. Furthermore, the presence of papilledema on ocular exam can support the diagnosis as well.[4] Certain clues to a patient's history should raise red flags that warrant further investigation. Examples include repeated visits to an acute care setting for new or worsening headaches, oral contraceptive use, pregnancy or postpartum state, and malignancy, among others.

If a CVST is suspected, transfer to a tertiary care center must be done immediately for further imaging, as MRI and magnetic resonance venography are the initial tests of choice for diagnosis. Most often, clots are found in multiple locations, but the super sagittal sinus and the transverse/sigmoid sinuses are the most frequently involved areas.[6]

Treatment of cerebral venous thrombosis includes systemic anticoagulation as a first-line agent. The American Stroke Association recommends unfractionated or low molecular weight heparin with eventual bridging to warfarin.[7] The novel anticoagulants have not been thoroughly studied in CVST and thus are currently not recommended in treatment guidelines. However, they are currently being studied outside the U.S. and may potentially replace warfarin in the near future. Mechanical thrombectomy is a potential treatment for severe venous sinus thrombosis or when anticoagulation is contraindicated. Failure to recognize and treat CVST not only delays the diagnosis, but worsens prognosis.

Most patients require treatment with anticoagulation alone. However, some patients require endovascular thrombolysis or more invasive procedures such as a decompressive craniotomy, which are done in clinical situations where patients quickly deteriorate despite anticoagulation.[8] Current advances in technology are promising with regard to finding quicker ways to reach a diagnosis. For example, there is a published manuscript on using bedside ultrasound to differentiate between a common headache from headache due to increased intracranial pressure.[9]

Resolution

Our patient had a provoked thrombosis secondary to oral contraceptives. Low doses of oral contraceptive still have elevated risk for thrombosis, and there are case reports of CVST with use of vaginal ring contraceptives as well.[10]

A majority of patients will have recanalization of the vessels after thrombosis, but, as in this case, some

Table 1. Etiology in Men and Women

Etiology	Women (n=465)	Men (n=159)	P value
Gender-specific risk factors	65%	NA	NA
Oral contraceptives	46%	NA	NA
Pregnancy or puerperium	17%	NA	NA
Hormone-replacement therapy	3%	NA	NA
Complete etiological workup	79%	82%	0.5
No risk factor identified	8%	25%	<0.001
More than one risk factor identified	47%	33%	0.003
Genetic thrombophilia	22%	25%	0.4
Acquired prothrombotic condition	16%	15%	0.7
Any infection	10%	21%	<0.001
Ear, nose, and throat infection	7%	13%	0.03
Central nervous system infection	2%	4%	0.1
Malignancy	6%	11%	0.03
Mechanical precipitants	3%	8%	0.04

Mechanical precipitants includes cranial trauma, neurosurgical intervention, jugular catheter occlusion, and lumbar puncture; acquired prothrombotic condition includes nephrotic syndrome, antiphospholipid antibodies, and hyperhomocysteinemia.
Adapted from Coutinho JM, Ferro JM, Canhão P, et al. Cerebral venous and sinus thrombosis in women. *Stroke*. 2009;40(7):2356-2361.

patients will have chronic occlusion with formation of collateral circulation.[4] This patient initially presented to urgent care for severe positional headaches but was diagnosed with atypical migraine and was sent home with instructions to follow up with her primary care provider. This scenario is very common, and patients with CVST will often present with headaches, yet the diagnosis can be easily missed due to the rarity of the case and complexity of its presentation. Thus, knowledge of its presentation, risk factors, and common findings is very important in order to avoid delays in diagnosis and avoid life-threatening outcomes.

After 3 months of warfarin use, the patient continued to have occasional episodes of headache without any visual changes or focal neurological deficits. Repeat magnetic resonance venography at 3 months showed chronic occlusion of the superior sagittal sinus and right transverse sinus. The sigmoid sinus had recanalized. ■

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Teaching Points

- Although rare, CVST is an important differential for a patient with risk factors for thromboembolism. The most important risk factors for CVST are pregnancy and puerperium, oral contraceptive use, thrombophilia, malignancy.
- If patient is showing signs of increased intracranial pressure, they should be sent to the emergency department for further workup.
- Remember the red flags: repeated visits to an acute care setting for new or worsening headaches, oral contraceptive use, pregnancy or postpartum state, and malignancy, among others.
- MRI/MRV are the tests of choice for diagnosing CVST and first-line therapy is with anticoagulation.