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Ultrasound in Emergency Medicine

CEREBRAL VENOUS THROMBOSIS: AN UNCOMMON CAUSE OF PAPILLEDEMA ON BEDSIDE OCULAR ULTRASOUND

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☐ **Abstract—Background: Cerebral venous thrombosis (CVT) is a rare, difficult-to-diagnose form of venous thromboembolic disease and is considered a type of stroke. Its presentation is highly variable and may be easily confused for more common and less debilitating or life-threatening diagnoses such as migraine, seizure, or idiopathic intracranial hypertension. Case Report: A 25-year-old woman presented with a complaint of bifrontal throbbing headache and blurry vision. A bedside ultrasound of the orbit suggested increased intracranial pressure. A subsequent computed tomography venogram demonstrated a left transverse sinus thrombosis. The patient was started on enoxaparin and admitted for bridging to warfarin and evaluation for hypercoagulable state. Why Should an Emergency Physician Be Aware of This?: CVT is a rare form of stroke that carries a high rate of mortality and morbidity and masquerades as more common and benign diagnoses. Emergency department bedside ultrasound of the orbit may make the diagnosis of CVT more attainable by identifying patients with increased intracranial pressure.** **© 2018 Elsevier Inc. All rights reserved.**

☐ **Keywords—cerebral venous sinus thrombosis; dural venous thrombosis; cerebral venous thrombosis; headache; intracranial hypertension; papilledema; optic nerve sheath diameter; POCUS; ocular ultrasound**

INTRODUCTION

Cerebral venous thrombosis (CVT) is a rare, difficult to diagnose, and highly mortal form of thromboembolism. Patients may present acutely, subacutely, or chronically, and complaints may masquerade as an arterial occlusion or as one of a multitude of more common and benign emergency department (ED) diagnoses such as migraine, seizure, or idiopathic intracranial hypertension. Diagnosis of CVT often occurs only after repeated presentations.

The following case report describes the use of bedside ultrasound to differentiate a common headache from a headache due to increased intracranial pressure (ICP). To our knowledge, this is the first published case of the use of ED bedside ocular ultrasound to detect increased ICP due to CVT.

CASE REPORT

A 25-year-old African American woman with no past medical history presented to our ED with a complaint of a bifrontal throbbing headache associated with bilaterally blurry vision for 7 days. She reported that the headache had begun insidiously and progressively worsened. She denied any known inciting event and reported that the headache was not maximal at onset and denied positionality or temporality. Additionally, she reported the headache was unaccompanied by photophobia, nausea, vomiting, neck stiffness, diplopia, fever, or chills. She denied any recent illnesses and reported there was no known personal or family history of

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subarachnoid hemorrhage or polycystic kidney disease. She reported her only medication was an implanted contraceptive.

Her recurrent and severe headaches had developed only during the previous few months, and for this reason she found these headaches concerning. She had presented to another hospital with this complaint twice in the previous month. However, a cause for her headache had not been found. Records from the outside hospital showed that the patient had presented with the nearly identical complaint approximately 1 month prior to our evaluation and was admitted for intractable headache. During her admission she underwent extensive neuroimaging. A computed tomography (CT) scan of the brain obtained at that time was interpreted as normal. A CT angiogram of the brain showed fenestration of the right proximal M1 segment of the middle cerebral artery without aneurysm, an infundibulum to left internal carotid artery communicating segment, and narrowing of the lateral transverse sinuses. A magnetic resonance imaging (MRI) study with and without contrast at that time showed diffuse vascular enhancement thought to be due to either motion artifact or leptomeningeal enhancement. Neurology and Neurosurgery were consulted and concluded that these findings were likely normal variant. She was treated as status migrainosus with steroids, ketorolac, antiemetics, and magnesium, and was discharged after complete resolution of her headache.

On examination, her vital signs were normal, with the exception of a heart rate of 105 beats/min. She appeared to be a well-developed, thin woman who appeared uncomfortable but nontoxic. Neurological examination, including cranial nerves, strength, sensation, cerebellar function, and ambulation were normal. HEENT (head, eyes, ears, nose, and throat) examination was normal. Her eye examination was notable only for mildly decreased visual acuity at 20/25 bilaterally. A bedside ocular ultrasound, performed in lieu of fundoscopy, demonstrated bilateral papilledema and enlargement of the optic nerve sheath diameter (ONSD) to 6.6-mm OD (right eye) and 6.2-mm OS (left eye) (Figures 1 and 2). The remainder of her ocular examination was normal.

The patient was provided prochlorperazine, diphenhydramine, and acetaminophen, after which her headache resolved. A complete blood count and basic metabolic panel were normal. A urine pregnancy test was negative. A CT venogram was obtained and demonstrated a left transverse sinus thrombosis (Figures 3–5). She was started on enoxaparin, and Neurology was consulted for admission for bridging to warfarin and evaluation for hypercoagulability.

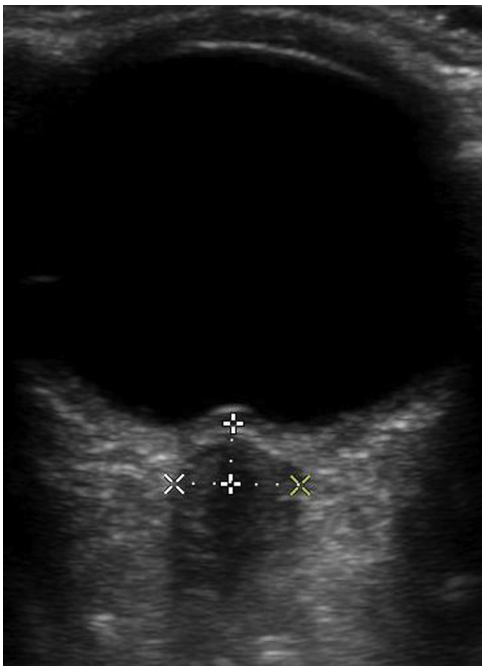

Figure 1. Transverse view of the right eye demonstrating widening of the optic nerve sheath and optic disc height elevation.

DISCUSSION

Background and Presentation

CVT, also known as dural venous thrombosis, is a rare and diagnostically challenging type of thromboembolic disease that is considered a form of stroke. CVT

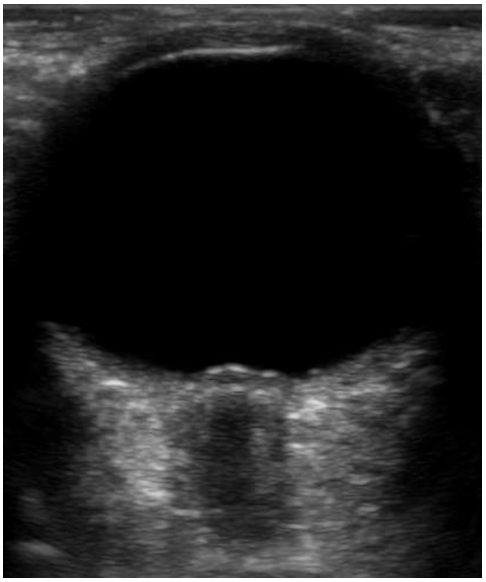

Figure 2. Transverse view of the left eye demonstrating widening of the optic nerve sheath and optic disc height elevation.

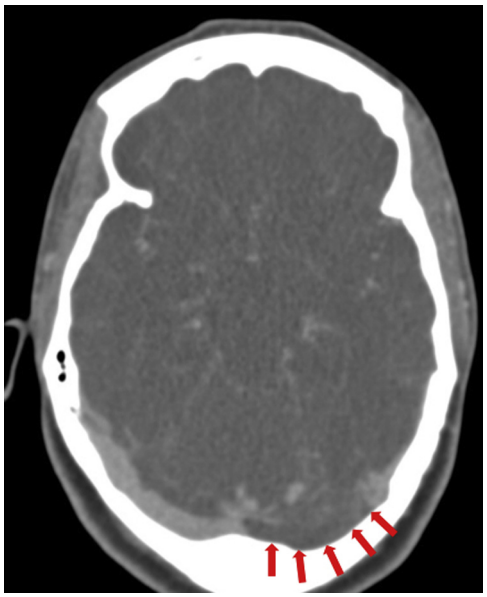

Figure 3. Axial cut computed tomography venogram demonstrating a thrombus within the left transverse sinus (red arrows).

represents 0.5–2% of all strokes and has an estimated incidence of 3–5 per million people annually (1,2). The young are disproportionately affected, with 78% of cases occurring in those under age 50 years (1). Presentations are highly variable and may include headache, focal neurological deficits, seizures, intracranial hemorrhage, papilledema, isolated psychiatric disturbances, tinnitus, or encephalopathy (1–3). The time from onset of features until diagnosis is also highly variable. Only 30% are discovered within 2 days of onset. Between

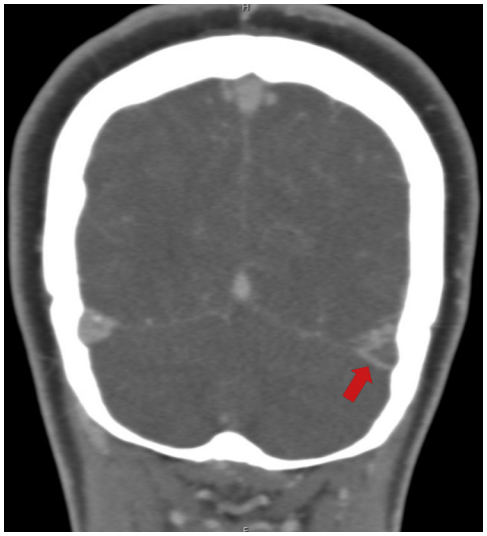

Figure 4. Coronal cut computed tomography venogram showing an empty delta sign within the left transverse sinus (red arrow).

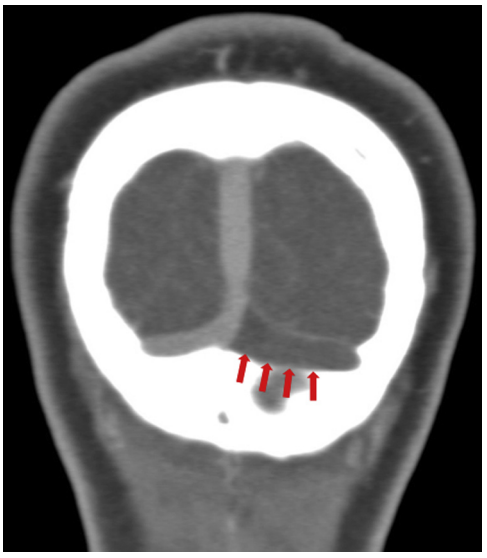

Figure 5. Coronal cut computed tomography venogram at the level of the confluence of the transverse and sagittal sinuses demonstrating a filling defect in the left transverse sinus (red arrows).

40% and 50% of cases are subacute, with symptoms present for 2 to 30 days. The remaining 20–30% are discovered in the chronic phase, with > 30 days of symptoms (4,5).

Historically, CVT was thought to result from infection of the head and neck, however, contemporary imaging suggests that infection is responsible for < 10% of cases among adults (1–3). However, 40% of children in one series had CVT attributed to infection (1). It is now believed that the causes of CVT are multifactorial. Inherited thrombophilia, malignancy, intracranial masses, pregnancy, trauma, infection, and exogenous hormones are all recognized as risk factors, demonstrating the considerable overlap between CVT and other venous thromboembolism diseases (1,3). However, the discovery of one risk factor should not preclude the search for others as 44% of patients have more than a single risk factor (3). No cause is identified in 15–25% of cases (2,6).

CVT leads to venous congestion, limiting cerebral blood flow as the differential between arterial and venous flow decreases. This may result in cerebral edema, venous infarction, or hemorrhage (6). Headache is thought to occur as a result of increased ICP, distension of dural nerve fibers, and local inflammation (3,5).

Headaches occur in 90% of cases and are most commonly described as generalized and progressive (1). However, description of the headache is variable and has been described as thunderclap or migraine with aura in some cases (3). In 25% of cases, headache, without any neurological abnormality or papilledema, is the only presenting feature (1). Because headache is the

initial symptom in 70% of cases and the dominant symptom in 90% of cases, CVT should be considered as a diagnostic possibility in all patients presenting to the ED with a complaint of headache (6).

Papilledema refers to swelling of the optic disc as a result of increased ICP (7,8). Elevation of the disc due to underlying local causes is referred to as pseudopapilledema, papillitis, or, simply, optic disc or optic nerve edema. The first sign of papilledema is obscuration of the disc margin, hyperemia, and loss of spontaneous retinal venous pulsations. In time, the elevated ICP that accompanies papilledema can result in flame-shaped hemorrhages due to overpressure and cotton wool spots due to ischemia (7). Some emergency physicians are not confident in their ability to accurately perform and interpret fundoscopy. Fundoscopy by direct ophthalmoscopy is technically challenging and difficult to interpret in the absence of focused and repeated practice (9). One study examining the ability of physicians to identify papilledema on photographs of fundoscopy found the sensitivity for papilledema to range from 73.2% to 85.2%, and the specificity ranged from 59.3% to 85.3%, depending on physician medical specialty (10). Furthermore, papilledema takes time to develop, and for this reason is noted in only 50% of cases of CVT (5). Despite this, > 80% of those with CVT who undergo lumbar puncture have an elevated opening pressure (1).

The Role of Bedside Ultrasound

The frequency of elevated opening pressure provides emergency physicians an opportunity to increase the probability of diagnosing CVT rapidly, accurately, and noninvasively through the use of point-of-care ultrasound. Bedside ocular ultrasound is a core competency of ultrasound training for current U.S. Emergency Medicine trainees. Ocular ultrasound has been used to evaluate retinal detachment, vitreous hemorrhage, ocular lens dislocation, papilledema, and optic nerve sheath widening (11). Ultrasound has been suggested as an alternative to fundoscopy in evaluation of papilledema (12). Optic disc elevation is identified on ultrasound as an indentation into the vitreous at the normally smooth contour of the posterior globe where the optic nerve meets the retina (Figure 6). Optic disc elevation > 0.6 mm above the posterior surface of the globe is 82% sensitive and 76% specific for clinically diagnosed papilledema. A cutoff of 1.0 mm is 73% sensitive and 100% specific (13). The relative infrequency of papilledema among patients with CVT makes optic disc elevation less clinically useful.

The use of ultrasound to evaluate for dilatation of the optic nerve sheath is a well-established surrogate for

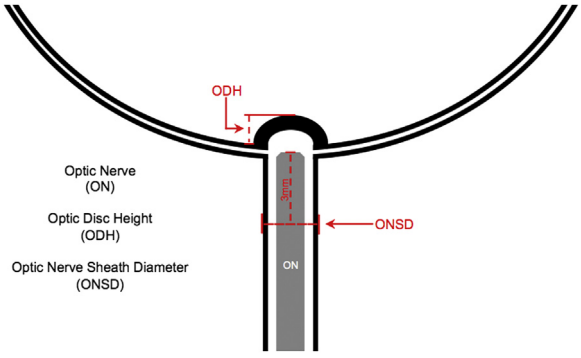

Figure 6. Diagram of the posterior of the eye demonstrating the proper location for measurement of optic disc height and optic nerve sheath diameter.

elevated ICP. Because increased opening pressure is common among patients with CVT, using ocular ultrasound to screen for evidence of increased ICP may facilitate earlier detection of CVT by emergency physicians. The optic nerve is an extension of the central nervous system and the optic nerve sheath is an extension of the meninges (14). The space between the optic nerve sheath and the optic nerve is a direct communication of the subarachnoid space (15). Studies using ultrasound to compare patients with idiopathic intracranial hypertension to controls have shown a statistical difference in ONSD with no difference in the diameter of the optic nerve (16). In human studies, using a manometer to directly measure the subarachnoid space beneath the optic nerve sheath corresponds to known positional changes in ICP within seconds. This suggests that there is no resistance conferred by the optic canal (17). Additionally, the ONSD has been demonstrated to increase in size in relation to increased ICP within an hour in animal models (18). On ultrasound, the optic nerve is a linear, hypoechoic structure that inserts into the globe. Surrounding the nerve is the hypoechoic optic nerve sheath. Sandwiched between these two structures is the trabecular, hyperechoic subarachnoid space. The subarachnoid space may not necessarily be visible among those with normal ICPs.

The ONSD is measured 3 mm posterior to the lamina cribrosa (Figure 6) (14). The ONSD is measured at this point because this is the point at which the optic nerve sheath is maximally distensible (19). The average of the ONSD of both right and left is used to assess for evidence of increased ICP (14). The nerve and sheath should be perpendicular to the probe and measured at the maximal diameter to prevent foreshortening and minimizing false negative measurements.

Multiple studies have investigated the ideal cutoff for ONSD to screen for increased ICP. Two studies determined that ONSD was 100% sensitive and 63–95% specific for CT evidence of increased ICP at a cutoff of 5 mm

(15,20). Studies evaluating ONSD as a measure for lumbar puncture opening pressure have used different cutoffs for opening pressure and ONSD. One study found an ONSD larger than 5.5 mm to be 100% sensitive and 100% specific to detect an opening pressure ≥ 20 cm H_2O (21). Another found an ONSD > 6.3 mm to be 94.7% sensitive and 90.9% specific for an opening pressure ≥ 25 cm H_2O (14). A study comparing ONSD to external ventricular drain showed that an ONSD > 5 mm was 88% sensitive and 93% specific for an ICP ≥ 20 cm H_2O, whereas an ONSD > 4.5 mm was 100% sensitive and 63% specific (22). One author has suggested interpreting an ONSD < 5 mm as normal, > 6 mm as reflecting increased ICP, and the range from 5–6 mm requiring clinical correlation (23). It is thought that there is a ceiling to the capacity for dilatation of the ONSD at approximately 7 mm (24).

Advanced Imaging

The diagnosis of CVT is typically confirmed with advanced imaging. The reference standard for diagnosis has historically been traditional angiography (5). Today, noncontrasted CT of the head (NCHC) is commonly the first type of neuroimaging obtained in acute neurological emergencies. Thirty-eight percent of NCHCs will be normal in those with acute CVTs (2). However, 8% of those with CVT will demonstrate focal edema and one-third will demonstrate parenchymal hemorrhage on NCHC (25). Acute thrombus may be seen within the venous sinuses as increased attenuation in 20–25% of cases (4,25). A dense triangle sign may be seen as increased attenuation in transverse view of a dural sinus, and a cord sign may be seen as increased attenuation of a cortical vein (4). Unfortunately, increased attenuation may also be seen in dehydration, elevated hematocrit, or near hemorrhage (25).

Unenhanced MRI is more sensitive for CVT than noncontrasted CT (25). MRI findings depend upon the age of the thrombus and are thought to be due to changes in oxygenation of hemoglobin and iron within the thrombus. Additionally, unenhanced MRI may show indirect signs of CVT such as venous congestion on apparent diffusion coefficient imaging and thalamic edema. However, MRI has multiple limitations in the diagnosis of CVT. Acute findings may show subtle abnormalities that may be easily missed. Flow-related enhancement may falsely suggest a thrombus. Lastly, paramagnetic components of a CVT may also mimic normal flow (2).

Most commonly, the diagnosis of CVT relies on MR or CT venography. However, normal variants of anatomy such as sinus atresia or hypoplasia, asymmetric drainage, arachnoid granulations, and intrasinus septations may mimic CVT (25). MR venography (MRV) may be obtained with gadolinium contrast or without, and use of time-of-flight techniques. Gadolinium-contrasted MRV is considered superior to time-of-flight MRV. Combo-4D MRV is considered to be 97% sensitive and 99% specific for CVT (2). Limitations to MR venography include cost, artifact due to movement, availability, and contraindications to MR such as presence of indwelling medical devices sensitive to magnetic forces. Further, MRV has more equivocal findings than CT venography (4). CT venography is superior to MRV in providing a more detailed view of the cerebral venous system (25). Contrast-enhanced CT venography may demonstrate a triangular filling defect within the transverse or sagittal sinuses known as an empty delta sign in 25–75% of cases (4). Compared with digital subtraction angiography, CT venography is 95% sensitive and 91% specific for diagnosis of CVT (6). One study comparing multidetector-row CT venography to MRI and MR venography demonstrated CT venography to be 100% sensitive and 100% specific for CVT (26). The American Heart Association and American Stroke Association suggest that either CT venography or MRV should be obtained if there is concern for CVT (1). Downsides of CT venography center on radiation exposure and contraindications to contrast (25). In pregnancy and in children, shared decision-making regarding the risks and benefits of CT and MR venography should be considered. If high suspicion of CVT exists and either MR or CT venography is inconclusive, then catheter cerebral angiography is indicated (1).

Treatment and Prognosis

A patient with a newly diagnosed CVT may be admitted to a stroke unit for monitoring for decompensation and investigation of underlying cause. In the absence of hemorrhage, anticoagulation with either unfractionated or low-molecular-weight heparin followed by vitamin K antagonists is indicated (1). Most guidelines recommend vitamin K antagonist use for 3–12 months. There is insufficient evidence to support the use of direct oral anticoagulants such as factor Xa and direct thrombin inhibitors (6). Among those who deteriorate despite anticoagulation, endovascular intervention may be considered (1). If intracranial hemorrhage is present, anticoagulation should be held and neurosurgical consultation should be obtained. Patients who present with or develop seizures should receive an antiepileptic (1,3). Treatment with acetazolamide, lumbar puncture, or surgical diversion of cerebrospinal fluid should be considered if vision is threatened (3). Treatment with steroids is associated with increased death and dependence. Therefore, they are not recommended, even in the setting of focal brain

lesions, unless other underlying disease processes require them (1).

The mortality rate in the acute phase of CVT ranges from 3–15%, largely due to hemorrhage, multiple lesions, or diffuse edema leading to herniation. In the long term, complete recovery is thought to occur in 79%. Depending on the study, dependency ranges from 5.1–28% of cases. Overall mortality rate is thought to be between 8.3% and 9.7% (1).

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

CVT is a rare and diagnostically challenging disease that carries a sizeable morbidity and mortality burden. Classic teaching has held that CVT presents as either a focal neurological defect or a seizure in the setting of a head and neck infection. However, CVT is now known to present more commonly as a headache, and may have a normal physical examination, including neurological evaluation. Additionally, emergency physicians should maintain a high level of suspicion for CVT among patients presenting to the ED with a complaint of headache. Additionally, emergency physicians should consider screening patients with headache with bedside ocular ultrasound to assess for evidence of increased ICP. Point-of-care bedside ocular ultrasound has a high utility toward diagnosing a state of increased ICP, which causes papilledema. Therefore, ultrasound can be an important component of a diagnostic strategy targeted at enabling the diagnosis of causes of headache that are due to elevated ICP, such as this case of CVT.

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