Case Report

Cerebral venous sinus thrombosis in pregnancy presenting with hemiplegia: A case report

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A B S T R A C T

Cerebral venous sinus thrombosis (CVST) is a rather uncommon disorder. CVST is potentially lethal, therefore early detection and treatment is critical. CVST has been linked to pregnancy and puerperium, while COVID-19 infection has been linked to a hypercoagulable state. CVST can be difficult to detect and treat due to the wide range of neurological manifestations, especially in patients with hypercoagulability. The goal of this study is to conduct a literature review and present a unique case of a pregnant woman with CVST who had left hemiplegia and headache. After 6 months of treatment in the hospital, the patient’s hemiplegia was fully resolved. Here, we discuss the treatment of CVST in pregnant women who have a suspected past COVID-19 infection.

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Background

Cerebral venous sinus thrombosis (CVST) represents an uncommon condition encompassing approximately 1% of all cerebrovascular accidents with an annual incidence of 5 per million [1,2]. Previously, CVST has been difficult to identify; however, with the advent of magnetic resonance imaging (MRI) and angiography (MRA), it can now be reliably diagnosed. The disease is marked by clotting of blood within cerebral veins or dural sinuses, which generates blockage of venous outflow. This can lead to venous congestion as well as cerebral edema. The high capillary pressures favor hemorrhagic transformation, complicating this condition more frequently when compared to other ischemic processes [3]. Early diagnosis and treatment are essential, as prompt manage-
ment may save a patient’s life and avert further permanent disabilities.

CVST was previously attributed to central face cutaneous infections, otomastoid, and orbit infections. After the introduction of antibiotics, the main etiology has shifted to a hypercoagulable state. Nevertheless, the etiology of CVST is multifactorial, and co-existing risk factors are commonly involved in the initiation of the disease. Other important risk factors include pregnancy, malignancy, rheumatological disease, nephrotic syndrome, medications (such as oral contraceptive pills), sickle cell anemia, and many endocrine disorders including diabetes mellitus and thyroid disorders [1]. Additionally, there is a considerable female predominance among young adults as 70%-80% of cases are in women of childbearing age and within the general population, women experience more than 3 times the incidence of CVST when compared to men [1,2].

Pregnancy and puerperium are known risk factors for venous thrombosis and CVST. This is due to a host of physiological changes associated with pregnancy. Changes in maternal coagulation factors concentrations as levels of factors I, V, VII, VIII, IX, X, XII, and vWF rise while total levels of the anticoagulant protein S decline and evidence of resistance against protein C exists during pregnancy. The increase in total intravascular volume, the estrogen-mediated increase in vascular compliance, the contribution of progesterone and relaxin to systemic vasodilation, and the increase in venous capacitance all promote venous stasis and predispose to the formation of venous thrombi. A poorly studied factor worth mentioning is pregnancy-related changes in inflammatory cytokine levels which may play a role in the increased risk of thrombosis [4].

Meanwhile, COVID-19 infection has been well established for resulting in a hypercoagulable state. There is an overwhelming amount of evidence supporting this, the incidence of pulmonary thrombosis in COVID-19 infected patients was as high as 79% [5]. The rates of reported thrombotic events are different between ICU and non-ICU patients, 31-79% and 9.2-15% respectively [5]. Vascular endothelial injury, pro-inflammatory cytokines, complement, the release of serum procoagulants such as tissue factor expression, and downregulation of fibrinolytic pathways have been shown to be involved in the pathogenesis [5].

Given the diverse and varied neurological presentations, cerebral venous sinus thrombosis (CVST) can be challenging to diagnose and treat, especially in patients with no clear risk factors for hypercoagulability.

**Case presentation**

A previously healthy 22-year-old primigravid woman at 10 weeks’ gestation presented to the emergency department (ED) with a chief complaint of a headache for 7 days duration. Her symptoms of left-sided headache were associated with nausea, non-bloody non-bilious vomiting, and previous history of similar episodes. She improved with Paracetamol, Metoclopramide, and intravenous fluids. A computed tomography (CT) head without contrast was unremarkable. She was discharged and advised to return to ED if symptoms persist or worsen. The following day upon waking up, the patient developed decreased sensation and weakness on her left side, blurry vision, and worsening of her headache, which prompted her to return to the ED. The patient was conscious, alert, and oriented, and her vital signs were stable. Physical examination revealed a motor strength of one-fifth in both the left upper and lower limbs, and decreased sensation in the left face and left upper and lower limbs. There were no cerebellar signs, dysarthria, or cranial nerve deficits. The patient was admitted and a stroke code was activated.

A repeat CT head scan without contrast revealed an abnormal increased density involving the sagittal sinus which was absent in the previous study. There was no acute hemorrhage or mass effect. Findings were highly suggestive of CVST. Patient then underwent an MRI scan with MRA-MRV protocol. The MRI showed peripheral T1 hyperintensity of the superior sagittal sinus with corresponding gradient echo hypointensity worrisome for sinus thrombosis. There was no evidence of acute infarction, focus of restricted diffusion, vascular edema, mass effect or midline shift. The ventricles were normal in size and morphology. MRA was negative for occlusion or stenosis in the brain or carotids. In the MRV, there was absence of flow in the superior sagittal sinus consistent with thrombosis (Fig. 1). There was cortical vein thrombosis associated with it at the vertex. The transverse sinuses were not clearly visualized but this was deemed to be artifactual rather than additional thrombosis.

Patient was deemed not to be a candidate for TPA as she was outside of treatment window or endovascular intervention at that time after consulting neurointerventionalist. The patient received subcutaneous enoxaparin at therapeutic dosing twice per day. EEG revealed focal slowings in the left hemisphere concerning of mild focal cerebral dysfunction. Acquired and hereditary hypercoagulability workup was unremarkable. But the patient was found to be positive for COVID-19 antibodies, and we believe an asymptomatic infection has contributed to her disease process. The patient was discharged to a subacute rehabilitation center where she received physical therapy. After a period of 6 months, the patient completely recovered and had return of full neurological function and muscular strength. Repeat imaging demonstrated the resolution of her thrombosis (Fig. 2).

**Discussion**

The differential diagnosis of headache during pregnancy is broad and is most likely of primary nature. The most common causes of headaches in pregnancy are tension headaches and migraine. But when headaches change in character, intensity, or have associated new-onset neurological deficits, this strongly suggests a secondary origin. Secondary headaches in pregnancy include stroke, subarachnoid hemorrhage, reversible cerebral vasoconstriction syndrome, and cerebral venous sinus thrombosis [6].

The diagnosis of CVST is challenging because of its rarity, and highly variable clinical presentation and the symp-
toms can often be confused with other common pregnancy complaints (such as headache, lethargy, nausea, and vomiting). These factors also contribute to delays in the diagnosis. Pregnancy-related strokes occur in 30 out of 100,000 deliveries and CVST encompasses approximately 9.1 out of these cases [7]. Mortality from CVST is approximately <15% with in-hospital mortality of 6% [2]. The frequency is highest during the third trimester and postpartum as approximately 75% of pregnancy-related CVSTs occur in the postpartum period with the highest risk in 1-4 weeks after delivery [4]. It is worth noting that CVST might occur months after the delivery, as late as up to 3 months post-delivery [1].

The most common presenting symptom of CVST is headache (90%–97% of CVST presentations in the general population and 73% in the pregnant population). During pregnancy and the puerperium, CVST can also present with obtundation (40%), motor weakness (35%), seizures (48%), and visual disturbances (27%) [4]. The mean duration of symptom onset until diagnosis was found to be 5.9 days in systematic review [2]. Patients who present with a headache exclusively have a much more favorable prognosis. The previously mentioned systematic review of CVST in pregnancy and puerperium demonstrated that the mean age of patients at presentation was 26.5 years [2]. Of these patients, (36%) were pregnant and (64%) were postpartum [2]. Seventy percent of these patients were primigravid, as was our patient. This highlights the inference that risk of CVST might be increased during first pregnancies. Concurrent thrombophilia was elicited from patient history or further lab studies only in 38% of the patients [2].

Diagnosis can be confirmed with either CT venography or MR venography. Unenhanced MR is more sensitive for the demonstration of the venous thrombus and the occluded dural sinus or vein when compared to unenhanced CT [8]. Edema, ischemic hypodensity, and bleeding are examples of indirect radiological signs (signs of the empty delta and of the cord) [3]. Hyperdensity of the sinuses and cerebral veins causes the cord sign, which appears early (typically within 2 weeks, in deep or cortical veins) [3]. The empty delta sign is a delayed (presenting after 2 weeks) indicator of a triangular hypodensity that is not enhanced by contrast and is
most typically seen near the superior sagittal sinus [3]. Lumbar puncture findings include elevated opening pressure, and cerebrospinal fluid abnormalities such as elevated cell counts and protein [9]. Fibrin split products (D-dimer) may support the diagnosis, but if there is a strong clinical suspicion of CVST, a normal D-dimer level should not preclude further evaluation [4]. The thrombi in CVST are most frequently localized to the superior sagittal, transverse/sigmoid sinuses, and less frequently in the deep venous system. Although most often, patients present with thrombi involving multiple sites of the venous sinus system [2].

Evaluating the management of CVST in pregnancy is vital since the dynamics of pregnancy present unique challenges and restrictions to therapy. A systematic review of all published cases of CVST in pregnancy demonstrated that 91% of patients were treated with anticoagulation, while a minority of patients were treated with thrombolysis and/or thrombectomy. Intracranial hemorrhage occurred in 4 of the 66 patients, and all of them had received both anticoagulation and thrombolysis [2]. Importantly, CVST with associated intracranial hemorrhage should still be treated with anticoagulation [10]. In the Berlin and Dutch trials, 34 (43%) had an intracerebral hemorrhage at baseline and none of the patients randomized to heparin developed a new intracerebral hemorrhage. Three individuals who were given the placebo had a new intracerebral hemorrhage. This approach is in line with the theory that CVT hemorrhage is caused by a combination of venous outflow blockage and extremely high intradural and intravenous pressure, resulting in venule rupture and hemorrhagic transformation of venous infarctions [11].

For most patients with CVST, anticoagulation with subcutaneous low molecular weight heparin is recommended since it stops the progression of thrombosis and allows the endogenous anticoagulation systems to maintain vascular patency [3]. The European Stroke Organization guidelines suggest using LMWH instead of UFH [12]. There are no clear recommendations for thrombolysis for acute CVST, except that patients with a low pre-treatment risk of poor outcome should avoid aggressive treatments including thrombolysis. Endovascular intervention may be indicated for selected patients with CVST who develop progressive worsening of neurologic symptoms despite adequate anticoagulation with subcutaneous LMWH or intravenous heparin, endovascular thrombolysis [11]. Additionally, mechanical thrombectomy may be a treatment option at centers experienced with these methods in addition to LMWH [11].

Complications that can occur during the acute phase include elevated intracranial pressure and seizures. Decompressive surgery, as well as other measures to reduce acutely elevated intracranial pressure and approaching herniation, may be required [7]. The benefit of seizure prophylaxis is uncertain due to the low likelihood of recurrence should seizures occur, but seizure prophylaxis is recommended for patients presenting with seizures and focal cerebral lesions. For patients with focal brain lesions but no seizures, seizure prophylaxis is not recommended [11].

Even though this condition can be worsened by ischemic progression or bleeding, the cellular disruption is generally reversible, and patients with appropriate therapy have a good prognosis, even when a decompressive craniectomy is required [3]. Clinical status at the time of treatment is the most predictive factor of excellent outcomes in pregnant and puerperal patients with CVST, and thus therapy should be initiated before clinical deterioration. This emphasizes the utility of recognizing common CVST signs and symptoms. In a study mentioned earlier, patients with headache alone at the time of treatment were 3.9 times more likely to achieve long-term excellent outcomes and patients treated after deterioration to a comatose state were 3.6 times more likely to suffer long-term clinical deficits [2].

Factors associated with higher mortality include age above 40, the involvement of deep venous systems, more than 2 mural sinuses involved, and delay of treatment for more than 12 hours [3]. Pregnancy-related CVST can achieve comparable recovery rate at 12 months after anticoagulant therapy with non-pregnancy-related women [13]. Very little is known about the relapse rate during pregnancy and puerperium in women with a history of CVST: In pregnant women, UpToDate recommends temporary preventive anticoagulation with subcutaneous LMWH during pregnancy and for up to 8 weeks after delivery [11].

Conclusion

CSVT was reported in only a few pregnancy cases to present with hemiplegia and asymptomatic COVID-19 infection. Risk factors for CVST include genetic or acquired hypercoagulability as well as pregnancy, puerperium, and other diseases [1]. COVID-19 increases the risk for thrombotic events and strokes [5]. According to the guidelines of the European Federation of Neurological Societies, thrombolysis is the first-line treatment for CVST. Treatment for CVST is still controversial and needs extensive research. Nonetheless, LMWH has been studied as a safe and effective treatment during pregnancy [13]. Newer oral anticoagulants (eg, Apixaban) might offer an easier alternative to traditional therapies for CVST but there is no evidence supporting their use. Physical therapy should be provided for all patients.

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Patient consent

As this is a case report, consent was obtained for the purpose of this paper.
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