

# Cerebral Venous Sinus Thrombosis as a Rare Complication of Hyperemesis Gravidarum: A Case Report

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**Abstract Objective:** Cerebral venous sinus thrombosis (CVST) is an uncommon but serious sequelae of severe hyperemesis gravidarum. Pregnancy and puerperium are important risk factors for CVST. Here, we report a case of CVST induced by hyperemesis gravidarum. **Case report:** A 25-year-old Palestinian woman, gravida 3, para 2 in the first trimester of her pregnancy. The patient was first diagnosed with severe hyperemesis gravidarum due to recurrent episodes of nausea and vomiting. As the condition advanced, the patient had headache and generalized weakness for a one-week duration. Neuroimaging revealed extensive thrombosis in the cerebral sinuses; thereby CVST was diagnosed. The patient was treated with anticoagulant and had a complete recovery. **Conclusion:** Although rare, it is important to include cerebral venous sinus thrombosis (CVST) in the differential diagnosis of any brain syndrome during all trimesters of pregnancy and puerperium. In this case study, we affirm the significance of suspecting CVST in pregnant women complaining of any neurological syndrome, especially in the setting of severe hyperemesis gravidarum.

**Keywords:** cerebral venous sinus thrombosis, severe hyperemesis gravidarum, pregnancy, puerperium, neuroimaging, anticoagulation

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## 1. Introduction

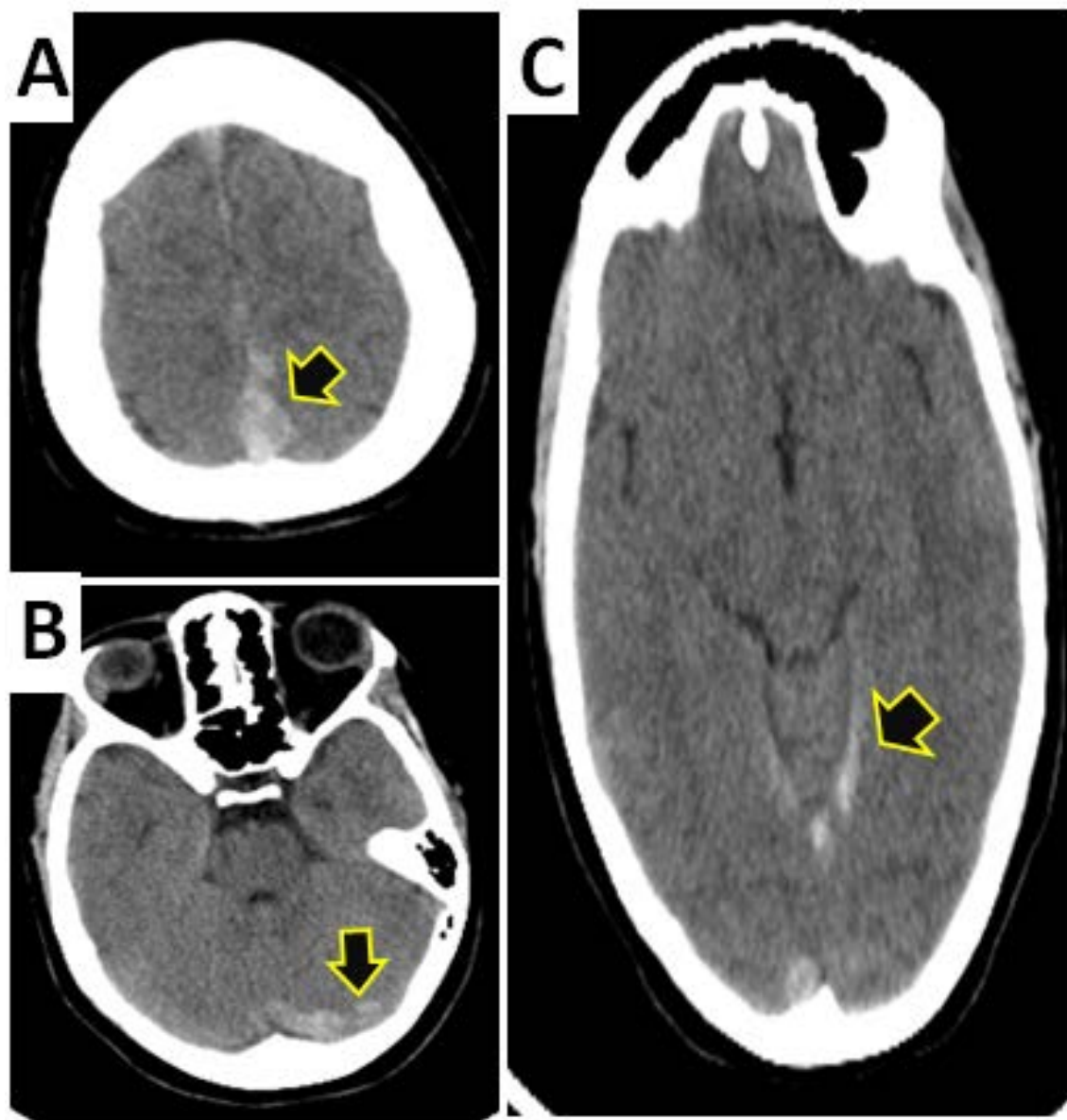
Cerebral venous sinus thrombosis (CVST) is a rare and serious condition. CVST is caused by complete or incomplete occlusion of the cranial sinuses and/or cerebral venous network and is responsible for 0.5-1% of all cerebrovascular accidents [1]. CVST tends to be more common in women compared to men, notably between the 20 and 35 ages. This gender predilection is rationally attributable to gender-specific risk factors (GSRF) including pregnancy, puerperium, hormonal treatment, and/or contraceptive usage [2]. The condition is also more prevalent in young individuals and those with parenchymal diseases [3]. CVST is characterized by incredibly variable and/or life-threatening clinical manifestation; thus, high clinical suspicion index is required [4,5]. The most frequent presentation of CVST is headache. Patients may also experience nausea, emesis,

seizures, visual disturbances, and/or other neurological impairments [1,2]. Together with the aforementioned GSRF, there are several risk factors that increase the possibility of CVST including hypercoagulable conditions, dehydration, infection, and cerebral ischemia [4]. Non-enhanced Computed tomography (CT) scan and Magnetic resonance imaging (MRI) are the preferred neuroimaging modalities for establishing the diagnosis. Anticoagulation is the prime CVST therapeutic option in clinical practice, as stipulated by the 2017 European ESO/EAN Guidelines [1]. According to pregnancy and puerperium periods, the vast majority of CVST cases occur in the third trimester and the first month following delivery [6]. Precisely, CVST seems to be 13 times more common in puerperium than in pregnancy. Even though it's uncommon, CVST can also be encountered during the early stages of pregnancy [2]. Herein, we report a very rare case of CVST diagnosed during the first trimester of pregnancy which is aggravated by hyperemesis gravidarum.

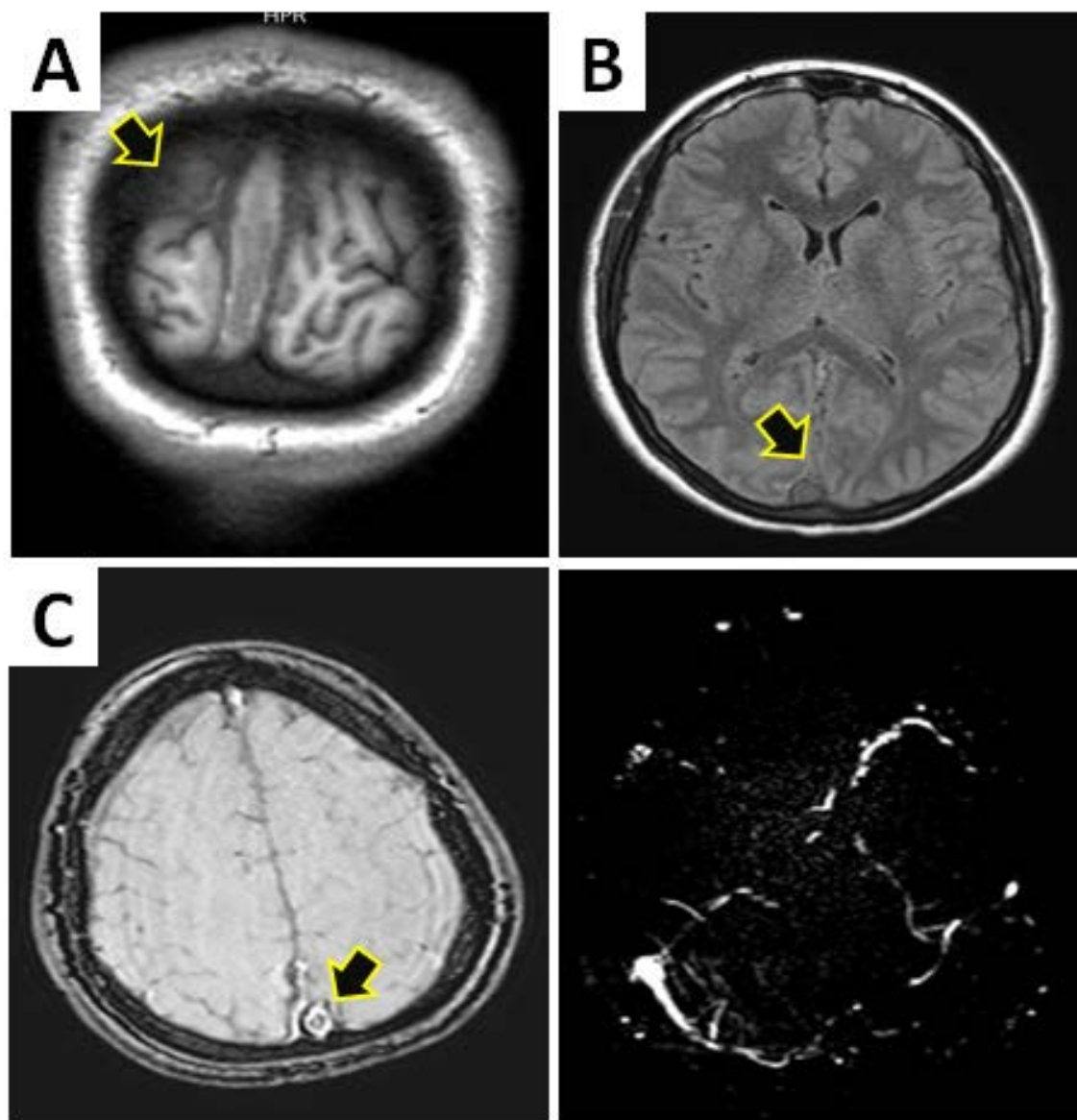
## 2. Case Report

N.J., a 25-year-old Palestinian woman, gravida 3 para 2 in her 8<sup>th</sup> week of gestation. On May 3<sup>rd</sup>, 2022, she presented to the Obstetric Department of Al-Makassed Charitable Society Hospital-Jerusalem. The patient had generalized weakness, severe, persistent headache, fever along with decreased appetite, nausea, and vomiting for a one-week duration. Prior to that time, the patient was repeatedly admitted into prenatal ward of our hospital due to sever recurrent episodes of nausea and vomiting and was diagnosed with hyperemesis gravidarum. The patient denied any previous traumatic events, oral contraceptive use, personal and/or family history of thrombophilia, malignancy, systemic inflammatory disorders, or autoimmune diseases. She had never experienced similar symptoms in her prior pregnancies. Upon admission, physical assessment revealed a critically ill patient with altered mental status, decreased level of consciousness, neck stiffness, and a high temperature of 38.4°C with stable other vital signs.

Neurological examination revealed no focal neurological deficit, photophobia, phonophobia, or abnormal movement. Kernig's and Brudzinski's signs were negative. Empirical antibiotics were prescribed. Laboratory evaluation including coagulation studies and investigations for connective tissue diseases were unremarkable. Lumbar puncture was unable to be performed as the patient was started on empirical enoxaparin due to our suspicion for thrombotic event. Computed tomography (CT) scan showed hyperdensity in the left transverse sinus, superior sagittal sinus, straight sinus and left sigmoid sinus, these findings are suggestive of a thrombotic event, (Figure 1). Magnetic resonance imaging (MRI) of the patient's head confirmed the diagnosis of Cerebral venous sinus thrombosis by disclosing of extensive thrombosis in the left transverse, superior sagittal, left sigmoid, straight sinuses, and internal cerebral vein (Figure 2). The Patient was treated appropriately with low molecular heparin and achieved complete recovery with an uneventful post-therapeutic period.



**Figure 1.** (A): is a computed tomography (CT) scan showing hyperdensity in the superior sagittal sinus, (B): is a CT scan showing hyperdensity in the straight sinus, (C): is a CT scan showing hyperdensity in the sigmoid sinus (arrows)



**Figure 2.** (A): is a Magnetic resonance imaging (MRI) T1, (B): is an MRI T2 showing thrombosis in the superior sagittal sinus, (C): is a Magnetic resonance venography showing absence of signal of part of superior sagittal sinus (arrows). (D): is an MRV maximum intensity projection showing thrombosis in the transverse sinus, sigmoid sinus and internal cerebral vein

### 3. Discussion

Cerebral venous sinus thrombosis (CVST) is an extremely rare and potentially fatal form of venous thromboembolism (VTE) which can be encountered during pregnancy and puerperal periods. It seems to be 13 folds more frequent during puerperium compared to the pregnancy, especially in the third trimester. The first trimester of pregnancy is very rare to be complicated by this drastic thrombotic event with an overall prevalence of 1.2/100000 deliveries [7]. Our patient experienced CVST during her 8<sup>th</sup> week of gestation. The most common presumed underlying mechanism of CVST in pregnancy is the fact that pregnancy itself is considered a hypercoagulable state which is aggravated by hyperemesis gravidarum that results in dehydration [7]. CVST begins with thrombus formation; this thrombus may undergo enlargement and cause venous occlusion and congestion. This will result in cerebral edema and mass-like effect with a resultant elevation of intracranial pressure. If not promptly managed, intracranial pressure will keep going up and

eventually exceed arterial blood pressure leading to cerebral blood supply compromise and subsequent ischemia. The international Study on Cerebral Vein and Dural Sinus Thrombosis revealed that 86% of CVST cases occur in the transverse sinus, 62% in the superior sagittal sinus, 18% in the straight sinus, 17% in the cortical veins, 12% in the jugular veins and 11% in vein of Galen and internal cerebral vein [5]. In our case, the superior sagittal, left transverse, straight, left sigmoid sinuses and internal cerebral vein were all involved.

Essential headaches, including migraines and tension headaches, are the most frequent causes of headaches during pregnancy. Notwithstanding, new-onset, worsening headache, and/or headache changing in its character should raise suspicion for secondary underlying causes such as cerebrovascular accidents (CVA), subarachnoid bleeding (SAH), brain tumors, CVST, reversible cerebral vasoconstriction syndrome (RCVS). Our patient presented with acute, sudden onset of persistent headache. The incidence of secondary headache increases in the pregnancy due to multiple factors including anesthesia use

during labor, increased tendency for coagulation, dehydration (such as hyperemesis gravidarum) as well as hormonal fluctuations [8,9].

The clinical manifestation of CVST is obviously variable depending on several factors including age of the patient, the underlying etiology, the location and extent of thrombosis. CVST patients may experience a constellation of complaints such as headache (87%), nausea and emesis (28%), seizure (24%), visual disturbances (27%), other neurological impairments (18%), altered mental status (18%), and cranial nerve palsies (18%) [5]. Other infrequent symptoms entail subarachnoid hemorrhage, transient ischemic attack and/or tinnitus [10]. Our patient had a constellation of generalized weakness, severe persistent headache, fever along with decreased appetite, nausea, vomiting, altered mental status, diminished level of consciousness, and neck stiffness.

Given its rarity and wide clinical presentation diversity, emergent diagnosis of CVST is particularly challenging. Therefore, high clinical suspicion index and perspicacity are mandatory for establishing the diagnosis. Laboratory evaluation including complete blood count, coagulation studies, and metabolic testing should be performed to recognize any underlying factor of CVST. Cerebrospinal fluid examination can also help in the exclusion of intracranial lesions. Elevation of D-Dimer may be a valuable diagnostic finding [11]. The gold standard diagnostic technique is brain neuroimaging, which is inevitably needed for diagnosis confirmation and detection of the exact site of CVST. The best initial neuroimaging test is a non-enhanced computed tomography (CT) scan [12]. Non-enhanced CT scan can enable direct visualization of thrombotic lesion (dense clot sign) and cord or string-like density (cord or string sign). These findings are termed as direct signs. Meanwhile, indirect signs include cerebral edema, midline structural deviation and/or intracerebral hemorrhage. CT scan with contrast can demonstrate a central area of minimal attenuation surrounded by contrast in a triangular shape (empty delta sign). 30% of patients may have normal or inconclusive CT scans; thus, unremarkable CT scan findings don't exclude CVST [13]. Magnetic resonance imaging (MRI) with contrast and magnetic resonance venography (MRV) remains the most favored diagnostic option for CVST, especially during pregnancy as it doesn't involve radiation exposure. 1.5-T magnet MRI is considered safe and can be used effectively to diagnose CVST during all trimesters of pregnancy. Cerebral angiography has been recently replaced by CT scan and MRI [14]. In our patient, the CT scan showed hyperdensity in the superior sagittal sinus, left transverse, straight, and left sigmoid sinuses that suggested CVST (Figure 1). MRI revealed extensive superficial and deep cerebral venous sinus thrombosis and diagnosis of CVST was confirmed (Figure 2).

According to the European Stroke Organization and the European Academy of Neurology (ESO/EAN) guidelines, the best first-line therapy for CVST is anticoagulation. Anticoagulants play an important role in the promotion of already formed thrombus to resolve leading to recanalization of the affected veins or sinuses, prevention of further thrombus formation, treatment of the predisposing thrombotic disorders and avoidance of possible consequences encompassing pulmonary thromboembolism (PE). Low

molecular weight heparin (LMWH) has been shown to be superior to unfractionated heparin in terms of mortality and functional results with comparable systemic bleeding risks. Moreover, the inability of LMWH to cross the placenta, which minimizes its adverse teratogenic effects. These features made LMWH the best anticoagulant therapeutic option for CVST in pregnant women. Interventional thrombectomy can be effective in non-responding patients to antithrombotic treatment [2,15]. The vast majority of pregnant women treated with anticoagulation had a good prognosis with a 5-10% mortality rate [7]. Our patient was treated successfully with LMWH enoxaparin with complete recovery.

## 4. Conclusion

Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening complication of hyperemesis gravidarum if misdiagnosed and/or left untreated. CVST mostly occurs in the puerperium and third trimester of pregnancy. However, it can also complicate the first trimester. Due to the rare incidence and wide variability of its clinical presentation, CVST can be easily overlooked during pregnancy. Therefore, clinicians should be very meticulous in recognizing this condition as early as possible. The diagnosis of CVST may be initially ambiguous and requires constant vigilance and greater effort due to its non-specific manifestations. Whenever it's suspected, neuroimaging is the best diagnostic modality of choice to detect CVST. Anticoagulation such as low molecular weight heparin is the first line of treatment.

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