

Cerebral Venous Sinus Thrombosis during Early First Trimester of Pregnancy

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Abstract: Cerebral venous sinus thrombosis is a rare condition. The most frequent symptoms and signs are headache, focal seizures with or without secondary generalization, unilateral or bilateral paresis and papilledema. We report a case of a 30-year-old woman; gravida-4, parity-3, at 8 weeks of pregnancy who was admitted for one episode of tonic-clonic seizures and altered sensorium. A magnetic resonance scan of her brain showed the presence of acute venous infarct magnetic resonance venography ultimately revealed left sigmoid, transverse and superior sagittal sinus and cortical vein thrombosis. The pregnancy was terminated and she was treated with low molecular weight heparin (LMWH) followed by warfarin. Though patient developed monoparesis later on and there was evidence of hemorrhagic transformation of the infarct, she had excellent recovery a few weeks after admission and was regularly followed up. Due to its diverse neurological presentation, cerebral venous sinus thrombosis should be considered in all brain syndromes even during pregnancy and should be treated with anti-coagulation.

Keywords: cerebral venous sinus thrombosis, early pregnancy, cerebral hemorrhage.

1. Introduction

Cerebral venous sinus thrombosis is a rare condition and its clinical presentation is extremely variable and life-threatening [1], [2]. The most frequent symptoms and signs are headache (95%), focal seizures with or without secondary generalization (47%), unilateral or bilateral paresis (43%) and papilledema (41%) [3]. Among its important etiological factors, pregnancy, puerperium, oral contraceptive use, coagulopathies, intracranial infections, cranial tumors, lumbar puncture, malignancy, dehydration, inflammatory bowel disease, connective tissue disorders, Behcet's disease, parenteral infections, and various drugs can be implicated [4]. Among other causes, the inherited pro-thrombotic tendencies, such as factor V Leiden mutation, protein S or C and anti-thrombin III deficiencies are also important. However, in 30% of patients the etiology cannot be determined [5].

Cerebral venous sinus thrombosis (CVST) accounts for 0.5-1.0% of all strokes [6]. During late pregnancy and puerperium, CVST is an uncommon but important cause of stroke [7]. Hemorrhagic infarction can occur in the acute stage of CVST. However, CVST with cerebral hemorrhage is extremely rare in early pregnancy. Upon literature review, we are able to find only few cases of CVST resulting in cerebral hemorrhage in early (first trimester) pregnancy [8], [9]. Treatment options for CVST include anticoagulants, thrombolytic therapy and, in some cases, surgical thrombectomy. The use of heparin and oral anticoagulants is based on a rationale of reversing the causal thrombotic process and of preventing complications [10]. CVST can result in death or permanent disability, but usually has a favorable prognosis [11]. Here, we present another case of

CVST with cerebral hemorrhage in early pregnancy, the patient received a favorable outcome by termination of pregnancy and use of anticoagulation therapy.

2. Case Report

A 30-year-old woman presented with acute onset of severe diffuse headache for one day and slurred speech for 4 hours. On presentation there was one episode of generalized tonic-clonic seizures. She was 8 weeks into her fourth pregnancy (gravida 4, parity 3). There was no history of fever, neck pain, blurring of vision and bowel-bladder complaints. There was history of taking anti-hypertensive drugs during her first pregnancy, which she did not require thereafter and stopped after medical advice. Other two pregnancies were uneventful. There was no history of epilepsy and other co-morbidities. She was not previously been on oral contraceptive pills, and did not have any personal or family history of venous thrombosis, autoimmune or hematologic diseases. She was brought to the hospital in postictal state and had altered sensorium for which we admitted her in intensive care unit. In the physical examination, there was no rise in temperature, no signs of meningeal irritation. She could move all limbs. Laboratory blood analysis was performed and the following results were obtained: Complete blood counts (Hb-10.8 gm%, TLC-6700/cmm, MCV-82.1 fL, Platelets-182000/cmm), serum glucose level-147 mg/dL, renal function tests (serum urea-15 mg/dL, serum creatinine-0.5 mg/dL), serum sodium (139 mmol/L) and potassium (4.8 mmol/L), liver function tests (Total Bili-0.70 mg/dL, SGOT-35 U/L, SGPT-9 U/L, ALP-68 U/L), ESR-32 mm at 1 hr, thyroid function (TSH-0.44 μ IU/ml, T3-4.04 ng/dL, T4-1.4 μ g/dL), PT-11.6 sec (INR-0.9), lipid profile tests (Total Cholesterol-183 mg/dL, TG-

99mg/dL, HDL-51mg/dL). MRI brain (1.5T scanner) done on admission revealed areas of restriction, diffusion was seen on DWI images in left frontal lobe with blooming in multiple areas on GRE images was seen suggestive of acute venous infarct (Figure 1 and Figure 2).

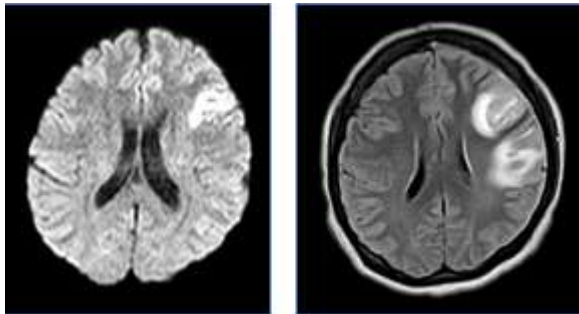


Figure 1 and Figure 2: DWI and Flair images showing blooming in multiple areas of left frontal lobe suggestive of acute venous infarct.

MR Venography revealed loss of flow seen in left sigmoid (Figure 3), transverse 2/3rd superior sagittal sinus and adjacent cortical veins appeared hyperintense on T1W images suggestive of acute cortical vein thrombosis. On fundoscopy there were no signs of papilloedema. To control intracranial hypertension, treatment with mannitol was administered immediately, and dose-adjusted low-molecular-weight heparin (60mg twice a day for five days) was started once the diagnosis of CVST was made. The seizures were controlled with intravenous Levetiracetam. To look for the other causes of CVST (other than pregnancy) we did investigate further. Anti-Phospholipid Antibody (APA) IgG and IgM were negative, Lupus Anticoagulants profile (LAC) including Cardiolipin + Beta2 Glycoprotein IIgM and IIgG were negative. Protein-S activity 87.9% (normal range: 60-130%), Protein-C activity 97.4% (normal range: 65-140%). Factor V Leiden- ratio 0.056 (slightly raised and jugular vein suggestive of thrombosis. Proximal). Neurophysician and obstetrician were consulted and after the consent obtained from husband the termination of pregnancy was performed (on day 5) to reduce the further risk to mother. The procedure was uneventful. MRI was repeated after five days. It was suggestive of recanalization in the left sigmoid sinus and jugular vein (Figure 4).

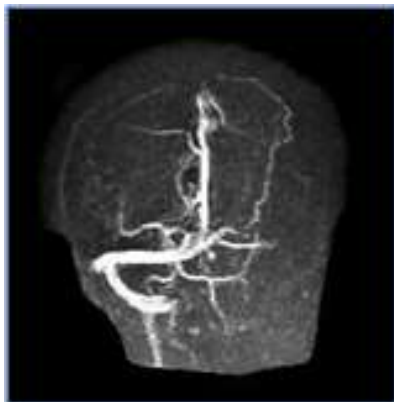


Figure 3: MRV showing obstructed flow seen in left sigmoid sinus



Figure 4: Repeat MRV suggestive of recanalization left sigmoid sinus and jugular vein

During the hospitalization, a bilateral headache was persistent. On the day after the termination of pregnancy she suddenly developed right upper limb weakness. Neurophysician's review was taken. CT scan brain was done which showed intraparenchymal bleed (left fronto-parietal lobe) in the same areas involving recent venous infarct without any significant increment in size (hemorrhagic transformation) (Figure 5). Anticoagulation was continued and Low Molecular Weight Heparin was replaced by oral Warfarin, 3mg once a day to maintain Prothrombin time between 2.0 and 3.5 times of control value (I.N.R.). During the course in the hospital the patient's right upper limb weakness spontaneously recovered within 48 hours. The patient had complete recovery and was discharged on warfarin and is on regular follow up with us.

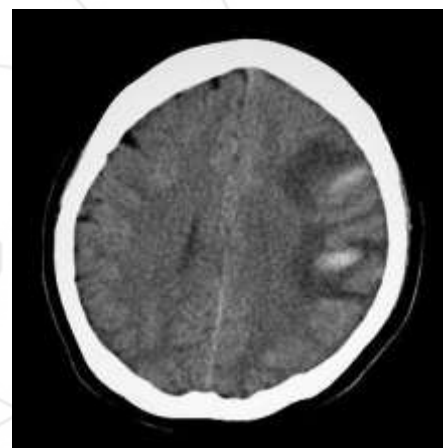


Figure 5: CT showing hemorrhagic transformation of acute infarct

3. Discussion

CVST is an uncommon but serious neurological emergency, the overall death, and dependency rate are approximately 10-15% [12]. Pregnancy and puerperium induces changes in the coagulation system, increasing the risk of CVST. The period of greatest risk for CVST includes the third trimester of pregnancy, and the first 4 postpartum weeks [13].

Only a few cases of CVST in early pregnancy have been reported [2], [8], [13], [14]. A CVST with cerebral hemorrhage in early pregnancy is extremely rare. The clinical manifestations of CVST are non-specific. The most frequent symptoms are headache, seizures, and decreased level of consciousness [15]. Based on the location of the thrombus, the patients may demonstrate focal neurological symptoms including hemiparesis, aphasia, sensorial loss, vertigo, dizziness. Signs of cerebral hernia can appear in patients with mass effects, such as edema, infarction, and

hemorrhage. Because of the wide spectrum of symptoms and signs of CVST, it can be difficult to arrive at the correct diagnosis based on clinical assessment alone. Our case was associated with the presence of worse prognostic factors as altered sensorium and focal neurological symptoms. This condition can be especially confused with eclampsia in patients with symptomatic severe preeclampsia. In case of development of additional neurological symptoms, CVST should be kept in mind together with other intracranial pathologies. Hemorrhage, infarction, edema can be detected on CT, a hyperdense lesion can be found occasionally in the venous sinus indicating thrombosis. However, CT is not recommended for pregnant women due to the radiation involved. An MRI can differentiate CVST from tumor apoplexy, and MRV can reveal sinus occlusion. Cerebral angiography is invasive and involves radiation; however, this method allows the detection of sinus thrombosis. Other vascular abnormalities such as aneurysm, arterio-venous fistula, and AVM can also be excluded by DSA.

The combination of MRI and MRV is the best choice for the investigation of suspected CVST in pregnant women. The CVST is an increasingly recognized neurological emergency. There have been no large trials of anticoagulation in pregnancy, and recommendations are based on case series and the opinions of experts. Anticoagulation is believed to be beneficial for patients with CVST and hemorrhagic complications and does not attribute to the deaths by causing hemorrhagic complications [16]. Although the best time to start anticoagulation treatment is not known, repeating CT or MRI to confirm that the intracranial hemorrhage is regressing or at least not progressing is advisable before starting anticoagulation. The use of endovascular treatment for CVST should be considered in patients who are resistant to anticoagulation therapy, have worsening symptoms, do not have intracranial hemorrhage, and are not at risk for impending herniation [17]. Decompressive hemicraniectomy could be life-saving and even lead to an excellent outcome in CVST patients with impending transtentorial herniation because of large hemorrhagic venous infarcts [18]. In patients with CVST in early pregnancy, early management of the embryo to eliminate the triggered spontaneous coagulation might also contribute toward recovery [13].

4. Conclusion

- 1) CVST with cerebral hemorrhage can occur in early pregnancy.
- 2) Its clinical manifestations may be non-specific as in this case. (patient had slurred speech, seizures, monoparesis).
- 3) An MRI combined with MRV may be the best choice for the investigation of a suspected CVST in a pregnant woman.
- 4) Anticoagulation therapy may be beneficial in curing CVST, even in pregnant patients with intracranial hemorrhage (hemorrhagic transformation) (In our patient, anticoagulation was successful when administered on the same day of the onset of the disease).

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