Case Report

Postpartum Thrombophilia- How Dangerous Is It?

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Abstract

Pregnancy and peri-partum period is characterized by a hypercoagulable state as part of physiological preparation for delivery in order to minimize blood loss during parturition. However these changes may at times result in increased risk of venous thrombosis commonly manifesting as cerebral venous thrombosis ('venous stroke'). In fact, 50% cases of cerebral venous thrombosis are reported in the peri-partum period. However, cerebral and peripheral venous thrombosis is rarely seen together in the absence of an underlying thrombophilic disorder. To highlight the importance of recognizing and treating venous thrombosis due to peri-partum hypercoagulable state, the following case of post-partum venous thromboses (peripheral and cerebral venous thrombosis) without underlying pro-thrombotic disorder is reported.

Introduction

Stroke in pregnancy and peripartum period are relatively rare. The incidence of stroke in non-pregnant women of child bearing age is 10.7 per 1, 00,000 women years, while it varies from 4.3 – 210 per 1,00,000 deliveries in pregnancy associated strokes. Though any cause of stoke in the young can coincidentally occur during and immediately after pregnancy, the specific causes related to pregnancy are eclampsia, postpartum cerebral angiopathy, ruptured cerebral aneurysm, cerebral venous thrombosis (CVT) and peripartum cardiomyopathy[1]. Arterial dissection, DIC, and stroke related to drugs (Bromocriptine, fertility and anaesthetic drugs) are other rarer causes[1]. A major cause of stroke in pregnancy is cerebral venous thrombosis ('Venous stroke') and over 50% of cases of CVT are associated with pregnancy or peurperium [2,3] Almost two-thirds of venous strokes associated with pregnancy occur in the third trimester or in peurperium . Pregnancy and peurperium are characterized by a hypercoagulable state, sometimes causing venous thrombosis, commonly affecting the dural or cerebral sinuses. Though venous stroke in peurperium carries more favorable prognosis, multiple and simultaneous cerebral and peripheral venous thrombosis is rarely seen. Here a case of post-partum venous stroke and deep venous thrombosis without an underlying thrombophilic disorder is reported.

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Case report

A young, 24 years old lady was brought on the 8th day post-partum with the complaints of headache, generalized tonic clonic seizures and weakness in the right lower extremity since 2 days prior to admission. She had a full term vaginal delivery 8 days prior to the hospitalization. There was no history of fever, ear discharge or projectile vomitting. There was no ante-partum history of excessive vomiting. There was no history of oral contraceptive use, recurrent abortions or similar complaints in the past. On examination, her vitals were stable and there were no signs of meningeal irritation. Fundus examination revealed early papilloedama. Central nervous system examination revealed hypotonia in the right leg with grade 0/5 strength, signs of hyper-reflexia in the form of exaggerated deep tendon reflexes in the right lower limb and ankle and patellar clonus with extensor plantar response. Other system examination was within normal limits.

Patient was investigated. Her routine investigations including complete blood count, kidney function test, liver function tests and coagulation profile were within normal limits. Her ECG, chest X-Ray and 2 D Echocardiography were within normal limits. MRI Brain was done which revealed superior sagittal sinus thrombosis with venous infarcts in the right frontal and bilateral parietal regions with hemorrhagic transformation with mass effect in the form of focal midline shift of about 1 mm **(Figures 1, 2).** She received injectable anti-coagulant therapy, anti-epileptics and anti-edema measures therapy.

Patient improved over the next 2-3 days; headache decreased and there was significant neurological recovery. However on the 4th day after admission, she complained of pain and redness over the right lower limb which extended

upto the thigh over the next 2 days. She had calf tenderness and Homan's sign was positive. Suspecting deep venous thrombosis (DVT), venous Doppler of the right leg was done which revealed acute deep venous thrombosis of mid and distal part of Sapheno-femoral vein, popliteal vein extending upto tibio-peroneal vein.Injectable anticoagulants was continued.

. Her repeat MRI Brain was done which showed partial recanalization of the superior sagittal sinus and significant reduction in the hemorrhage and cerebral edema. The thrombophilia screen of the patient was done which revealed normal levels of Homocystein, Protein C, Protein S and plasma Anti-thrombin III activity. Rheumatoid Factor, Anti-Phospholipid antibodies and Factor V Leiden were not detected. Test for PNH was negative. She was given Fondaparinux overlapped with Warfarin. Warfarin was later continued and INR maintained between 2.00 – 3.00. Repeat venous Doppler before discharge showed reduction in the thrombus dimensions with partial recanalization. Significant neurological recovery in the form of grade V power in the right lower extremity was there at the time of discharge.

Patient was discharged on Warfarin and anti-epileptics. Anti-coagulants were stopped after 6 months during which period she was asymptomatic.

Discussion

Many physiological, biochemical and anatomical changes occur during pregnancy in preparation for delivery resulting in a thrombophilic state to minimize blood loss during parturition. Increased concentration of coagulation factors[1,] progressive resistance to Protein C activity, reduced Protein S , increased concentration of Plasminogen activator inhibitors 1 and 2 occur during pregnancy. Additionally, hyperprolactinaemia of pregnancy causes increased platelet aggregability. Further contribution to venous thrombosis may occur due to venous stasis caused by illiac vein compression by the gravid uterus, prolonged bed-rest, infection and dehydration secondary to hyperemesis gravidarum or blood loss after delivery[1]. Endothelial injury, though uncommon in normal delivery, may occur during the course of vaginal or abdominal delivery. Thus all the three classic risk factors (venous stasis, endothelial injury and hypercoagulability) described by Virchow for venous thrombosis may occur during pregnancy.

The risk of peri-partum venous thrombosis increases with Caesarean delivery, increasing maternal age, increasing hospital size, and presence of co-morbid conditions like hypertension, infections other than pneumonia and influenza and excessive vomiting in pregnancy [3,]

Superior sagittal and lateral sinuses are the most frequently involved sinuses[1]. Patients with CVT usually present with headache, vomiting and papilledema due to raised intracranial tension secondary to increased venous pressure and impaired cerebrospinal fluid absorption. Headache and papilloedema alone are good prognostic signs. Rapidity of symptoms, early reduced Glasgow Coma Scale, focal neurological signs, seizures and concomitant infections are poor prognostic markers [4,]

The prognosis in peurperial CVT is better than other causes like malignancy, cerebral infarction or trauma, oral contraceptive use and thrombophilic disorders; probably due to transient and more limited occlusion and rapid recanalization or development of collaterals[2,] Maternal mortality rates are significantly lower than that for all-cause CVT. The usual cause of maternal death is secondary intracranial hemorrhage or hemorrhagic transformation [5]. Transtentorial herniation has also been reported to be fatal.[6]

The diagnostic modality of choice is MRI Brain; MR Venography may further support the diagnosis; though the typical presentation in the appropriate clinical setting makes the clinical diagnosis fairly easy. Search for underlying thrombophilic disorder should be undertaken as it decides the duration of treatment. Patients with thrombophilic disorders require life-long anticoagulants. However during an acute episode, false positive or false negative results may be observed. Patients on anticoagulants may also have faulty results. Hence patients should be off Warfarin for at least 2 weeks prior to these investigations.

The mainstay of treatment of CVT is Heparin, overlapped with oral anti-coagulants, which are later continued to maintain INR between 2.00 - 3.00. Anecdotal reports of successful endovascular thrombolysis have also been reported. The safety and efficacy of Heparin in CVT has been endorsed by previous studies [6,] Hemorrhagic venous infarction is not a contradiction for Heparin use. Endovascular thrombolysis with Urokinase, Streptokinase and recombinant tissue plasminogen activator have also shown beneficial effect [5]. However this conclusion has come from case reports, from highly specialized centers, carried out on the illest of patients and should be interpreted with caution, as this modality is invasive and potentially dangerous. Use of rheolytic catheter system to carry out mechanical thrombectomy has also been reported as a treatment modality.

To conclude, peri-partum pro-thrombotic state manifesting as CVT may be potentially dangerous and sometimes fatal. Though the prognosis of peri-partum CVT is relatively better than other causes, high degree of

suspicion, prompt recognition and appropriate management goes a long way in reducing the morbidity and mortality.

Source of Support: Nil

Conflict of Interest: None declared

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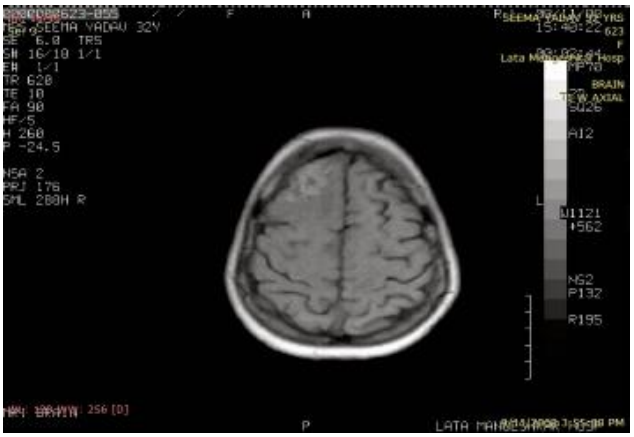

Figure 1
(T1 weighted axial) showing loss of normal flow voids in the superior sagittal sinus and venous infarcts (right frontal and bilateral parietal) with hemorrhagic transformation

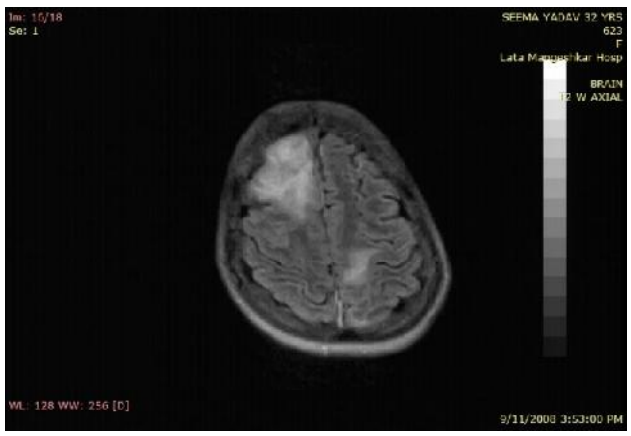

Figure 2.
T2 W axial image showing the same features as figure 1