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Case Report

Obstetrics and Gynaecology Section

Acute Cerebrovascular Accident in Pregnancy Due to Hyperhomocysteinaemia Secondary to Vitamin B12 Deficiency: A Case Report

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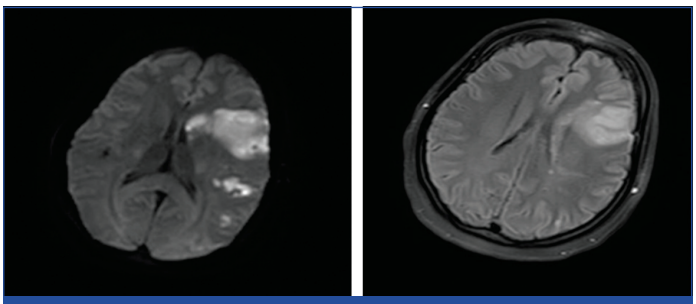
ABSTRACT

Stroke in pregnancy is rare but is one of the leading causes of morbidity and mortality in developed countries. Pregnancy, as a prothrombotic state, acts as a precursor for stroke. Preeclampsia, eclampsia, amniotic fluid embolism, hypertension, diabetes, and many other factors predispose to the development of stroke. Endothelial cell injury leading to arteriosclerosis, causing a stroke, has been associated with raised homocysteine levels. Hereby, the authors present a case of a 26-year-old Gravida 3 Pregnancy 1 Live 1 Abortion 1 (G3P1L1A1) at 35 weeks gestation with a cephalic presentation who complained of a headache for two days, sudden onset of weakness in the right upper limb and lower limb with an inability to walk without support and inability to speak since 12 hours, associated with one episode of vomiting. Magnetic Resonance Imaging (MRI) brain showed acute infarcts in the left fronto-parietal lobes and capsule region with haemorrhagic transformation in the left frontal lobe. Serum vitamin B12 measured by Electroluminescence Assay (ECLA) was found to be low at 113pg/mL (normal range -191-771pg/mL). Serum homocysteine levels measured by enzymatic method were elevated at 46 umol/L (normal range 3-18 umol/L). A diagnosis at 34 weeks of pregnancy with acute cerebrovascular accident with right hemiparesis with Broca's aphasia due to hyperhomocysteinaemia secondary to vitamin B12 deficiency was made. Prompt diagnosis and treatment are known to decrease morbidity in women with cerebrovascular accidents. MRI brain with venogram is known to be the gold standard procedure in diagnosing stroke. Thrombolytic therapy has proven beneficial in the treatment of the disease and in preventing its progression. Prenatal and natal supplementation with folic acid/vitamin B12 in the first trimester of pregnancy prevents Vitamin B12 deficiency and raised homocysteine levels in the maternal serum, thereby decreasing the incidence of stroke.

Keywords: Aphasia, Hemiparesis, Homocysteinaemia, Pregnancy, Stroke

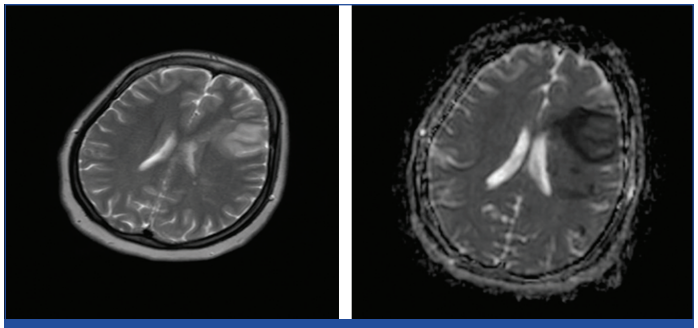
CASE REPORT

A 26-year-old G3P1L1A1 at 35 weeks gestation with a cephalic presentation and a history of a previous Lower Segment Caesarean Section (LSCS) presented to the Emergency Department with complaints of a headache for the past two days, a sudden onset of weakness in the right upper limb and lower limb with an inability to walk without support, and inability to speak for the past 12 hours, associated with one episode of vomiting. The patient had no history of loss of consciousness, syncope, or seizures. The patient is not a known case of hypertension, diabetes, ischaemic heart disease, or renal disease. Her blood pressure measured 130/90 mmHg. There were no signs of pallor, icterus, clubbing, cyanosis, oedema, or lymphadenopathy. Upon abdominal examination, the patient showed a gravid of 35-week size, relaxed, with no signs of scar tenderness, and a foetal heart rate of 146 bpm (beats per minute). However, on Central Nervous System (CNS) examination, the patient was conscious cooperative, and well-oriented to time, place, and person with the ability to comprehend and follow actions but with no word output. Her eye-opening response was normal, but her verbal response was indecipherable. Further examination revealed upper motor nerve weakness of the 7th nerve on the right-side. On the motor system examination, there was hypotonia with power 2/5 in the right upper and lower limbs. The right lower limb also showed a response to localising pain, bringing the Glasgow Coma Scale to 12/15. A neuro physician's opinion was sought regarding the same and diagnosed clinically with right hemiplegia with global aphasia. Investigation of the complete haemogram showed macrocytic anaemia with neutrophilic leucocytosis. Fundoscopy showed no evidence of papilledema or any other hypertensive retinopathic changes. MRI brain showed acute infarcts in the left fronto parietal lobes and capsule region with haemorrhagic transformation in the left frontal lobe [Table/Fig-1-4]. MR venogram showed hypoplastic inferior sagittal sinus, left transverse sinus, sigmoid sinus, and internal jugular vein. B/L carotid doppler showed soft plaque in the left carotid bulb extending into the proximal internal carotid artery. There was 15-20% luminal narrowing with no significant haemodynamic changes. A 2D echo showed normal valves with ejection fractions of 62%.



[Table/Fig-1]: Diffusion weighted image showing an infarct in left lobe.
[Table/Fig-2]: FLAIR image showing an infarct in left lobe. (Images from left to right).
FLAIR; Fluid attenuated inversion recovery

Serum vitamin B12 measured by ECLA was found to be low at 113 pg/mL (normal range-191-771 pg/mL). Serum homocysteine levels measured by an enzymatic method were elevated at 46 umol/L (normal range 3-18 umol/L). Ultrasound obstetrics revealed a single live intrauterine gestation of 34 weeks, weighing 2.37 kg with an Amniotic Fluid Index (AFI) of 11.



[Table/Fig-3]: T2 sequence showing haemorrhagic infarct in left lobe.
[Table/Fig-4]: ADC sequence showing infarct in left lobe. (Images from left to right).
ADC: Apparent diffusion coefficient

A diagnosis of G2P1L1 with 34 weeks of pregnancy with an acute cerebrovascular accident with right hemiparesis and Broca's aphasia due to hyperhomocysteinaemia secondary to vitamin B12 deficiency was made. The patient was started on anticonvulsants, Injection (Inj.) citicoline 500 mg 1-0-1, oral statins, and antiplatelet agents. As serum vitamin B12 levels were low, she was given Inj. vitamin B12 with vitamin B12 complex (Inj Optinueron). On day 2 of admission, the patient was stable, her speech improved, and she was shifted out of the Intensive Care Unit (ICU) and continued treatment with oral anticonvulsants, statins, and anti-platelets and started on tablet (Tab) folic acid 500 mcg. The patient improved symptomatically and was discharged on day 7 of admission. Her power in both limbs improved to 4/5 at the time of discharge, and she was advised to continue folic acid, vitamin B12 supplements, and Inj. vitamin B12 with vitamin B complex once weekly. After two weeks, the patient was admitted and underwent an elective caesarean section with no intrapartum or postpartum complications. The patient was asked to review after two weeks after surgery at the Department of Obstetrics and Gynaecology and followed upto six months. She has shown dramatic improvement and is asymptomatic at present.

DISCUSSION

Stroke is defined as a neurological deficit caused by an acute focal injury of the CNS due to a vascular cause, including cerebral infarction, Cerebral Vein Thrombosis (CVT), Intracranial Haemorrhage (ICH), and subarachnoid haemorrhage. The incidence of stroke in women of childbearing age is low, varying from 3.8 to 26 per 100,000 deliveries [1]. Pregnancy and the six weeks following childbirth are considered a prothrombotic state [2]. Hence, the incidence of stroke is said to be increased in the third trimester of pregnancy and the puerperal period [3]. Some conditions related to pregnancy like hyperemesis gravidarum, ovarian hyperstimulation, and preeclampsia are hypercoagulable states, thereby increasing the incidence of stroke [4]. Medical conditions associated with pregnancy such as anti-phospholipid syndrome, sickle cell disease, thrombotic thrombocytopenic purpura, haemolytic uremic syndrome, diabetes, mechanical heart valves, and cardiomyopathies increase the risk of ischaemic stroke [5]. Endothelial cell injury, platelet activation, thrombomodulin expression, protein C, and increased oxidisability of low-density lipoprotein have been reported as a few possible mechanisms by which homocysteine precipitates arteriosclerosis and thrombosis. Elevated homocysteine is a marker of low B vitamin levels in the individual or decreased methylation capacity of cells [6]. In present case, elevated homocysteine levels were noted. Hyperhomocysteinaemia is a risk factor for recurrent stroke and is associated with premature atherosclerosis [7]. Elevated homocysteine is a marker of low vitamin B12 levels in the individual or decreased methylation capacity of cells [8]. The incidence of vitamin B12 deficiency is predominantly seen in vegans, as seen in this patient, and the daily requirement of vitamin B12 in pregnant and lactating women is 2.6 mg/day [9].

Vitamin B12 deficiency can be associated with numerous causes, such as decreased intake, pernicious anaemia, and malabsorption syndromes. Deficiency of vitamin B12 prevents the conversion of homocysteine to methionine, causing the accumulation of homocysteine in the blood, which can predispose the patient to cardiovascular and cerebrovascular diseases, namely dementia, depression, acute psychosis, cerebrovascular accidents, myelopathy, and subacute combined degeneration [10].

Clinical examination and investigations are insufficient in the diagnosis of stroke. MRI is considerably safe in all trimesters of pregnancy and superior when compared to CT if done with a venogram [11]. MR studies may be useful in identifying CVT when combined with a venogram.

In a systematic review by Pinzon RT et al., the authors concluded that detecting hyperhomocysteinaemia and reducing homocysteine levels should be considered in women at risk for ischaemic stroke [12]. To authors knowledge, this is the first report of stroke during pregnancy caused by hyperhomocysteinaemia. There is no fixed protocol for managing stroke in pregnancy. Once haemorrhage is ruled out, ischaemic stroke should be managed with antithrombotic and antiplatelet agents as per standard guidelines for non pregnant women. Managing in a tertiary care hospital with a multidisciplinary approach will help to improve the prognosis [13]. Additionally, in present patient, with the correction of vitamin B12, a significant improvement was noted in the neurological function of the patient. No further episodes of stroke were noted during six months of follow-up.

Vitamin B12 supplementation prenatally and postnatally may have a role in preventing the elevation of homocysteine in pregnant women, thereby decreasing the incidence of stroke. Further studies will help to clarify and better manage cases of stroke in pregnancy.

CONCLUSION(S)

Although rare, the incidence and development of stroke during pregnancy and the puerperium have significant morbidity and mortality associated with the condition and can be exigent for diagnosing and managing the condition. Stroke in young individuals can be prevented with early diagnosis by identifying treatable risk factors, whether genetic or acquired. Stroke caused by hyperhomocysteinaemia with vitamin B12 deficiency is uncommon and a preventable cause of stroke. Therefore, a patient with a stroke in pregnancy should always be managed in a tertiary care hospital with specialised units and a swift multidisciplinary approach from an Obstetrician, Neurologist, and Radiologist.

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