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Case Report

Wernicke encephalopathy and extrapontine myelinolysis in pregnancy with hyperemesis gravidarum: a double jeopardy

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ABSTRACT

We report a case of a pregnant woman who had been suffering from hyperemesis gravidarum presented with alteration of consciousness, nystagmus, generalized weakness and extrapyramidal symptoms at 16th week of gestation. Magnetic resonance imaging of the brain showed typical findings of Wernicke's encephalopathy and extrapontine myelinolysis. The clinical features responded dramatically to high dose thiamine supplementation. Wernicke encephalopathy should be diagnosed as early as possible to prevent long-term neurological sequela or death as well as fetal loss.

Keywords: Hyperemesis gravidarum, Wernicke encephalopathy, Extrapontine myelinolysis, Central pontine myelinolysis

INTRODUCTION

Wernicke encephalopathy with extrapontine myelinolysis manifesting as extrapyramidal symptoms in coexistence is a rare occurrence in pregnancy with hyperemesis gravidarum with few case reports in literature.[1,2] We report the case of a pregnant woman with hyperemesis gravidarum who had clinical features and magnetic resonance imaging (MRI) findings of wernicke encephalopathy with additional features of extrapontine myelinolysis.

CASE REPORT

A 26-year-old gravida 2 with unremarkable medical history presented with altered mental status and generalized weakness at 16th week of gestation. Patient had history of intractable vomiting since 10th week onwards for which she saw a local practitioner and was given anti-emetics and intravenous fluids. However, her condition deteriorated and she developed unsteady gait, generalized weakness followed by altered mental status over a course of 2 weeks. At admission, patient was drowsy and disoriented with a Glasgow Coma score of 13/15. She was afebrile, her blood pressure was 110/70 mmHg with a pulse rate of 140/min. Her both pupils were equal and reactive to light, ocular fundus was normal. Multidirectional nystagmus was observed which was characteristically prominent in upbeat direction. As patient was unable to stand, she could not be examined for ataxia. Deep tendon reflexes were normal.

Laboratory investigations revealed serum sodium was 146 mmol/l (normal range 135-145 mmol/l), potassium was 3.1 mmol/l (normal range 3.5-5.0 mmol/l), pH was 7.55 sodium bicarbonate was 18.07 mmol/l (normal range 21-32 mmol/l). Her hemoglobin was 9.9 g%, total leucocyte count was 10,200 and platelet count was 2 lakh/cubic mm. Her renal function tests as well liver function tests were within limits. MRI brain showed T2/FLAIR hyperintense

signals in dorsomedial thalami, periaqueductal grey matter around third ventricle, bilateral caudate and lentiform nuclei. Mammillary bodies also appeared to be involved. Based on the finding diagnosis of wernicke encephalopathy with coexistent extrapontine myelinolysis was made. After three days of intravenous high dose thiamine supplementation (500 mg three times a day for 2 days followed by once a day for another 5 days), her clinical features significantly improved. Hyperemesis gravidarum was managed by rehydration, antiemetic medications and potassium replacement for hypokalemia. On her first follow up visit after a month, although she was improved considerably, she still needed assistance to walk and nystagmus was persistent.

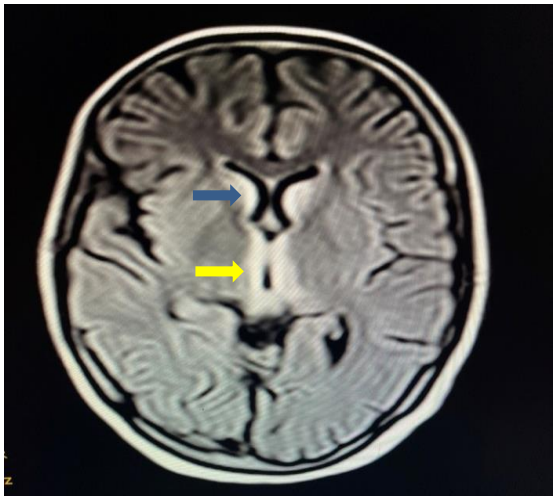

Figure 1: Axial T2 flair images of brain showing hypreintensities in periaqueductal grey matter (yellow arrow), tectum of midbrain, bilateral caudate nuceli (blue arrow).

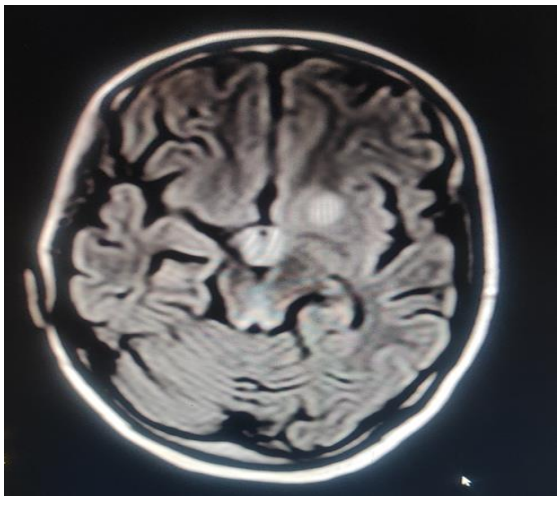

Figure 2: T2 hyperintensity in left lentiform nucleus.

DISCUSSION

Wernicke encephalopathy is an acute, neurological syndrome, characterized by nystagmus and/or ophthalmoplegia, mental status changes, and ataxic gait. It is an uncommon complication in hyperemesis gravidarum subsequent from the combination of poor nutritional status, frequent vomiting, and increased metabolic requirements of pregnancy. The diagnosis is made based on clinical presentation, and a definitive diagnosis is complicated as the clinical triad may not be present in up to 90% of patients.[3] It is a potentially reversible yet serious neurological manifestation caused by vitamin B_1 (thiamine) deficiency. Although commonly associated with heavy alcohol consumption, other associations are with hyperemesis gravidarum, starvation, gastrointestinal surgery and neoplasia. Thiamine pyrophosphate is the biological active form of vitamin B1; it is an essential coenzyme in many biochemical pathways in the brain, including transketolase, alpha-ketoglutarate dehydrogenase, and pyruvate dehydrogenase.[4] If the cells with high metabolic requirements have inadequate stores of thiamine, energy production drops, and neuronal damage ensues. The daily requirement of thiamine is around 1.1 mg/day for females, and it increases to 1.5 mg/day, particularly during pregnancy and lactation and even more by the impaired absorption due to hyperemesis gravidarum.[2]

Although wernicke encephalopathy is reversible, major complications can arise in the pregnant woman and the fetus. It can lead to permanent neurologic lesions and Korsakoff syndrome in the absence of active management, which is fatal in 10-20% of cases. It can also lead to miscarriage, preterm birth, and intrauterine growth retardation.[5] The diagnosis of wernicke encephalopathy is based on the clinical manifestations and rapid reversal of symptoms with thiamine. Although not readily available, determination of blood transketolase activity and thiamine pyrophosphate reflects the thiamine status in the body.[6] The typical lesions in MRI are symmetrical and located in the thalamus, mammillary bodies, tectal plate, and periaqueductal area; early reversible cytotoxic oedema is the most distinctive lesion.[7] If wernicke encephalopathy is suspected, treatment with thiamine, intravenously or intramuscularly, should be initiated immediately, and continued until a normal diet is resumed. Currently, there is no consensus about the optimal daily dose of thiamine treatment. Guidelines by the European Federation of Neurological Societies (EFNS) recommend that thiamine should be given 200 mg thrice daily via the intravenous route, before any carbohydrate, until there is no further improvement in signs and symptoms.[8] The Royal college of Physicians (London) developed comprehensive protocols for appropriate treatment, by using a high-potency vitamin B complex with minimum of thiamine 500 mg intravenously three times daily for 3 days; and, if clinical responded to treatment, continue daily thiamine 500 mg daily for 5 days or until clinical improvement ceases.[4] Chiossi et al in a review of 49 reported cases concluded that symptoms resolution required often months and complete remission is obtained in only 14 cases, spontaneous fetal loss rate was 37% and elective abortion rate was 10%.[2]

Several case reports illustrate that hyperemesis causing hypernatremia, hypokalemia, or hypophosphatemia eventually leads to osmotic demyelination in the form of central or extrapontine myelinolysis. Moreover, thiamine deficiency may render the myelin sheaths of central pons more sensitive to changes in serum sodium, phosphate, and potassium.[9]

In our patient, MRI brain showed hypersignal intensity signal in T2-weighted, DWI and FLAIR at dorsomedial thalami, periaqueductal grey matter around third ventricle, bilateral caudate, lentiform nuclei and mammillary bodies, however pons was not involved. These findings were compatible with wernicke encephalopathy and extrapontine myelinolysis. In extrapontine myelinolysis the pathological changes are identical to those of central pontine myelinolysis. Studies had shown that the extrapontine myelinolysis can occur with or without central pontine myelinolysis.[10] The lesions are often strikingly symmetrical. The age of lesions in the various sites in extrapontine is contemporaneous. Central and extrapontine myelinolysis are the same disease, sharing the same pathology, associations, and time course but differing in clinical manifestations. Typical pathology of central and extrapontine myelinolysis is characterized by loss of oligodendrocytes and myelin: however, the neurons and axons remain preserved.[11]

Other conditions associated with osmotic demyelination include chronic alcoholism (40%), rapid correction of hyponatremia (20%), post livertransplantation (17%), cirrhosis (5%) and hyperglycemia, malnutrition, azotemia, hypernatremia, and rapid normalization of hypophosphatemia.[12] In our case, extrapontine myelinolysis occurred probably due to hypokalemia, hypernatremia and hyperosmolality in hyperemesis. Long term management in these cases is largely supportive, which include ventilator support if required, intense physiotherapy and rehabilitation, and anti-parkinsonism drugs.

CONCLUSION

This case highlights the importance of early recognition of this potentially devastating condition and prompt initiation of thiamine supplementation. Wernicke encephalopathy is a potentially reversible condition if treated early. Moreover, replacement of electrolytes and glucose homeostasis is also important to prevent central and extrapontine myelinolysis (CPM and EPM). We would like to emphasize the importance of prompt thiamine supplementation especially before giving any glucose containing fluids and prevention of dyelectrolytemia in pregnant women with prolonged vomiting in pregnancy.

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