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Original Research Paper

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WERNICKE'S ENCEPHALOPATHY: A RARE COMPLICATION OF HYPEREMESIS GRAVIDARUM

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ABSTRACT Wernicke`s encephalopathy results due to severe thiamine deficiency; occurring mostly in chronic alcoholics. We present the case of 23-year-old female, at 15 weeks of pregnancy, with severe hyperemesis gravidarum. She presented with confusion, nystagmus, ophthalmoplegia, and ataxia. Clinically, presumptive diagnosis of Wernicke`s encephalopathy was made; very large doses of thiamine were administered to manage the case. A low serum thiamine level later confirmed the diagnosis. The patient was discharged home on day 16 with mild persistent up beating nystagmus. On follow up after 3 months, persistent up beating nystagmus with normal cognitive function and preserved memory was noted. Wernicke`s encephalopathy is a rare complication of hyperemesis gravidarum, if remained undiagnosed leads to long-term neurological sequela or death. Initiation of early thiamine replacement therapy in pregnant female with prolonged vomiting, will decrease maternal morbidity and foetal demise rate. Presently, only a few cases with this condition have been reported in the literature.

KEYWORDS : Hyperemesis gravidarum, Wernicke`s encephalopathy, thiamine, ataxia, nystagmus.

INTRODUCTION

In hyperemesis gravidarum (HG), long lasting and uncontrollable nausea and vomiting may lead to dehydration, ketosis, electrolyte abnormalities increasing maternal morbidity and mortality. Rarely HG complicates to Wernicke's encephalopathy (WE), a potentially fatal medical emergency due to thiamine deficiency. WE is a central neurological disorder manifests as the classic triad of encephalopathy, ophthalmoplegia, and/or nystagmus and ataxia[1]. WE is commonly seen in alcoholics but can also occur in any malnourished condition[2]. We report a rare complication of HG: WE.

CASE REPORT

A 23-year-old, primigravida, in her 15th week of gestation, with unremarkable medical history, started vomiting during the 6th week of pregnancy and treated with antiemetics but she continued to have persistent vomiting and developed generalised weakness. At 14th weeks of gestation, she was admitted to a private hospital for the similar complaints and treated with intravenous fluids including dextrose and antiemetics and referred to our tertiary care centre with obstetric ultrasound suggestive of single live intrauterine gestation.

On admission, she complained of blurring of vision and diplopia with confused mental state. She was oriented to person but not to time and place. On general physical examination cachexic appearance with signs of dehydration were noted. On ocular examination, pupils were bilaterally equal and reactive and ocular movements showed vertical nystagmus in both eyes. Ocular fundus showed flame shaped haemorrhages temporally on bilateral optic disc. On neurological examination we found loss of equilibrium with incoordination of gait and trunk ataxia with normal sensory system. Bilateral upper and lower limb power, tone and reflexes were within normal limits.

The blood pressure was 110/70 mmHg, pulse rate was 108/min, and respiratory rate was 16/min; the patient was afebrile with absence of pallor and oedema. Per abdominal examination showed 14-week size uterus with no organomegaly. Bedside Investigations showed urine ketones- large, urine sugar- nil, rBSL- 102mg/dl. Renal function tests showed no abnormality. Liver function tests showed L- aspartate aminotransferase level at 96 IU/L (Normal range (NR): <40) and L- alanine aminotransferase level at 84 IU/L (NR: <45). The serum potassium level was 2.3 mEq/L (NR: 3.5-5.5).

With confusion, nystagmus, ophthalmoplegia and ataxia in a case of HG with inadequate intake of thiamine, clinically provisional diagnosis of WE was made in this case. Blood for serum thiamine level estimation was sent to laboratory. Patient was started on parenteral thiamine 500 mg twice a day for two days followed by 250 mg twice a day and normal saline infusion. Intravenous potassium supplementation was also started. MRI brain was performed to rule out other intracranial causes, showed bilaterally symmetrical hyperintensities in medial and posterior thalamic and in periaqueductal area in T2 sequences, in fluid-attenuated inversion recovery (FLAIR), and in diffusion weighted imaging (DWI). Serum thiamine level was 40 nmol/L (NR: 70-200), hence confirmed the diagnosis of WE. After 6 days of parenteral thiamine therapy when she tolerated oral feeds, shifted to oral thiamine. Her neurological symptoms improved rapidly with the aggressive treatment, although nystagmus persisted. Missed abortion was detected on Obstetric ultrasound examination. She was aborted completely with PGE2gel induction with Foley's traction twice. She was discharged home on day 16 with persistent up beating nystagmus. The patient was re-evaluated from three months of diagnosis in our outpatient clinic and was noted to have a persistent up beating nystagmus. At this time, she had normal cognitive function and preserved memory with normal gait.

DISCUSSION

WE is a metabolic disorder as a result of thiamine (vitaminB1) deficiency. The prevalence of WE in a non-alcoholic patient varies from 0.04% to 0.13%. [9] It should be kept in mind in patients with anorexia nervosa, prolonged vomiting associated with chemotherapy, gastrointestinal disease, haemodialysis, and HG. [10] Thiamine is an important coenzyme in the Kreb's and pentose phosphate cycle. Its deficiency leads to focal lactic acidosis, cerebral energy impairment, and depolarization of neurons, prompting cell necrosis and apoptosis.[1] The human body has approximately 18 days of thiamine storage. During pregnancy, there is an increased thiamine requirement (1.1mg/day to 1.5 mg/day) and there may be impaired absorption due to HG. [2] In addition, intravenous dextrose infusion, frequently given in hyperemesis, leads to further depletion of thiamine reserve.

WE is primarily diagnosed on the basis of clinical grounds. Caine et al., reported that WE is diagnosed whenever there exist any two of the following four signs: Nutritional deficiencies, oculomotor abnormalities, cerebellar dysfunction, and/or either an altered sensorium or memory impairment.[3] In our case clinically had all of these four criteria: Prolonged vomiting, nystagmus, truncal ataxia, and was confused. Di Gangi et al., reported that the ocular signs, especially nystagmus, were present in 95.2% of the patients. The other signs included cerebellar signs in 82.5%; ataxia in 74.6%, confusion in 60.3%, hypotonia in 60.3%, memory impairment in 52.3%, and severe alteration of consciousness in 30.1% of the cases.[4] In a review of 49 cases of WE following hyperemesis gravidarum, the patient's mean (± standard deviation) age was 26.7 ± 4.9 years; WE manifested at a mean gestational age of 14.3 ± 3.4 weeks, and the mean duration of vomiting was 7.7 ± 2.8 weeks. The overall foetal death rate related to WE was 47.9% (23 of 49).[5] The clinical picture in our case matches these reported figures.

Our patient showed elevated liver transaminase levels. Rotman et al., suggested that patients with hyperemesis and elevated liver enzymes are more likely to develop WE than those with normal values. [6] Our patient also had hypokalaemia, which commonly accompanies hyperemesis. MRI is the imaging modality of choice in evaluating patients with possible WE because it is highly specific (93%). T2/FLAIR often shows bilateral symmetric hyperintensities in the mammillary bodies and medial thalami around the third ventricle, the tectal plate, and periaqueductal gray matter. DWI shows corresponding areas of restricted diffusion. [7] WE responds to therapy when there is involvement of only the periaqueductal regions, medial thalami, and caudate nuclei; the involvement of the cortical regions suggests irreversible damage and a unfavourable prognosis. [5] Our case showed the classic MRI findings of WE.

WE is treated by high doses of thiamine. Most authors recommend an intravenous dose, 500 mg per day given 4 times a day (q.i.d.) for 2 days. If an effective response is observed, 250 mg per day q.i.d. should be continued till the patient can tolerate oral thiamine. Then, oral thiamine should be continued, in a dose ranging from 60 to 100 mg daily for at least 3 months. [4], [8] In our case dramatic response to intravenous thiamine was noted, and neurological symptoms recovered in 3 days. This further confirmed the clinical diagnosis of WE.

WE leads to mortality in 10 to 20% of cases, however, neurological recovery in many patients is doubtful despite treatment. The symptoms start reversing in hours to days after thiamine replacement; the oculomotor signs improve first followed by imbalance and altered sensorium.[4],[8] Di Gangi et al., reported 34.5% spontaneous abortions, 9% elective abortions, and 3.6% foetal deaths in patients suffering from WE.[4]

CONCLUSION

Wernicke's encephalopathy can complicate HG though remains underdiagnosed. Early thiamine replacement ensures prompt recovery. Thiamine supplementation to any pregnant women with frequent vomiting should be considered. Here, early diagnosis and prompt treatment led to prevention of further complications. A multidisciplinary approach and risk counselling are needed.

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