CASE REPORT

A rare complication of hyperemesis gravidarum: Wernicke's encephalopathy

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Abstract

Wernicke's encephalopathy is a potentially fatal complication of hyperemesis gravidarum. It develops due to deficiency of vitamin B1 and presents with neurological signs dominantly. It is most frequently seen in alcoholics. In pregnancy, Wernicke's encephalopathy is a rare clinical condition difficult to diagnose and may prove to be fatal. Clinical and magnetic resonance imaging findings are useful in diagnosis. We report two cases of Wernicke's encephalopathy which were caused by prolonged hyperemesis gravidarum.

Keywords: Wernicke's encephalopathy, Vomiting, Hyperemesis, Thiamine.

Introduction

In hyperemesis (HE) gravidarum, long-lasting and uncontrollable nausea and vomiting may lead to dehydration, ketosis, hypochloraemia, and hypocalcaemia which may cause an increase in maternal morbidity and mortality. These pregnant women may uncommonly lead to Wernicke's encephalopathy (WE), which manifests with diplopia, amnesia, confusion, apathy, and vestibular paresia. Risk factors for WE are chronic alcoholism, previous gastrectomy, malnutrition, malignant diseases, transplantation and thiamine deficiency in the diet. WE caused by thiamine deficiency due to severe HE gravidarum, is reported uncommonly (0.1-0.5%).[1]

We report herein two WE cases induced by hyperemesis. One of these patients first had to be taken care of at the ophthalmology polyclinic because of visual deterioration.

Case Report

Case-1: A 34-year-old woman at 16 weeks' gestation visited the ophthalmology clinic for poor visual acuity. She was using an oral anti-emetic for the preceding six weeks due to nausea and vomiting. On examination, pseudotumour cerebri was suspected and she was directed to the neurology clinic. Following neurological examination, she was hospitalised with the diagnosis of 'pseudotumour cerebri in pregnancy'. Glucose-containing intravenous feeding was initiated due to longstanding vomiting, weight loss (5kg) and nutritional deficiency. Ten days later, in December 2010, she was referred to Izmir Ataturk Training and Research Hospital because of somnolence and late response to verbal stimuli. During the initial examination, she was found to be normotensive, confused and non-cooperative. Fundus uteri was observed at 20-22 weeks of pregnancy. In utero foetal death was detected by ultrasound. Laboratory studies showed: aspartate aminotransferase: 125 U/L (normal range, 5-34 U/L); alanine aminotransferase: 74 U/L (normal range, 0-55 U/L); γ-glutamyl transferase: 98 U/L (normal range, 9-36 U/L); creatine kinase: 511 U/L (normal range, 29-168 U/L). In addition, other laboratory test results were in the respective normal ranges.

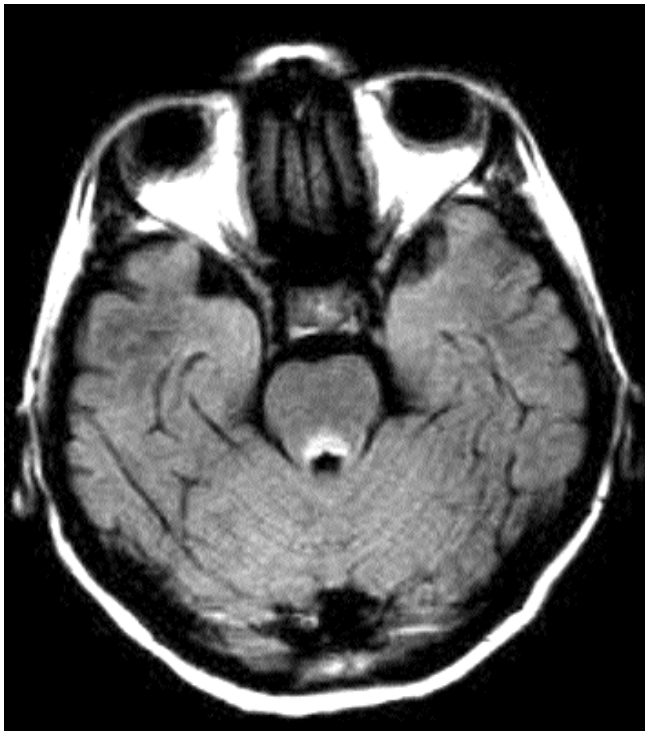

Figure-1: Wernicke's encephalopathy, FLAIR (Fluid-attenuated inversion recovery) axial scan: hyperintensity at the dorsal aspect of the brainstem, anterior to fourth ventricle.

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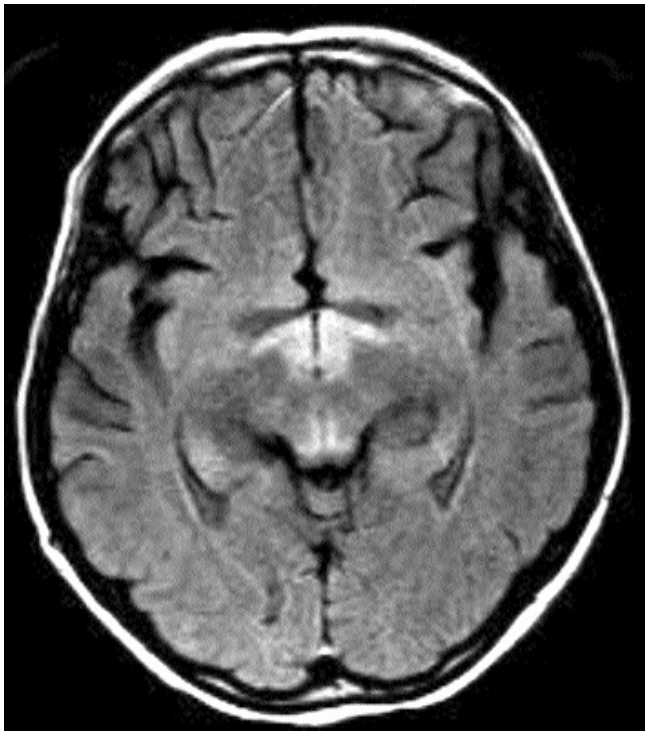

Figure-2: FLAIR axial sections; hyperintense symmetrical lesions seen in tegmentum, pons, mesencephalon, periaqueductal gray matter, hypothalamus, optic tract and the medial thalamus bilaterally.

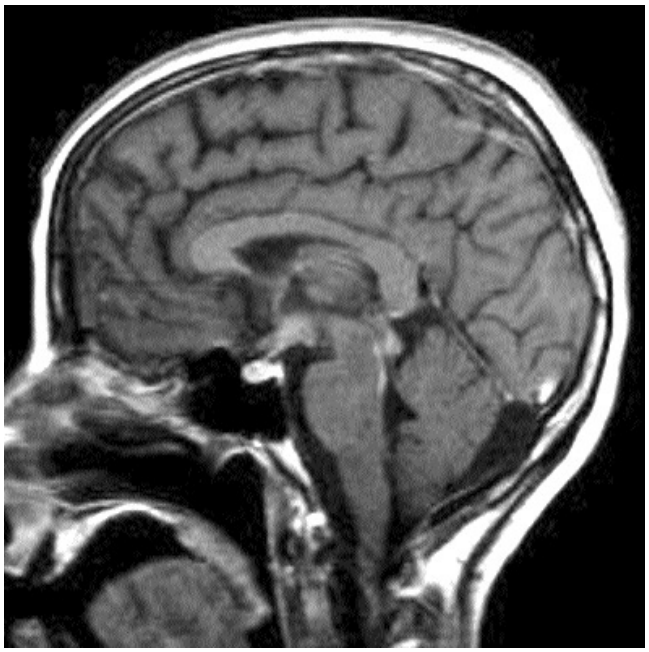

Figure-3: Post-contrast T1-weighted sagittal view of the hypothalamus, pituitary stalk, tectum and periaqueductal field with contrast enhanced areas.

Neurological examination revealed marked somnolence, disorientation and impaired short-term memory. Moreover, during ophthalmological examination bilateral visual loss, bilateral total ophthalmoplegia, vertical and horizontal nystagmus and at fundoscopy retinal haemorrhages and bilateral papillary oedema were detected. In the fluid-attenuated inversion recovery (FLAIR) and T2 sequences of cranial magnetic resonance imaging (MRI), bilaterally symmetrical hyperintensities were seen medial thalamic, periaqueductal gray matter and hypothalamic levels. Increased signal intensity areas were also identified in pons and mesencephalon. In post-contrast series, band or nodular hyperintensities were seen due to contrast enhancement at the hypothalamic area, pituitary stalk, periaqueductal region and tectum (Figure-1-3). Venous and arterial magnetic resonance angiography was normal. Electroencephalography (EEG) findings were consistent with encephalopathy. Pregnancy-induced WE was considered due to these findings and the patient was admitted to the intensive care unit (ICU) of neurology department. She was started on immediate intravenous thiamine replacement at doses of 100 mg/day.

Induction of medical abortion was performed by using intravaginal misoprostol 400 mcg 3 times a day. Response to induction by misoprostol was received within 24 hours. Subsequent to abortus, revision curettage was performed. Over the first 48 hours of thiamine therapy, consciousness status was recovered. Cooperation also improved, though speech was dysarthric. Extraocular eye movements began to recover within 72 hours. Vision loss and nystagmus started to decrease. On the fifth day, the patient was discharged from the ICU to the neurology unit. Ataxia improved from day 10 onwards. Ophthalmological re-examination performed on day 15 indicated that optic discs were within normal limits, retinal haemorrhages had decreased, visual acuity and colour vision was complete, while nystagmus persisted. After a month, MRI findings were evaluated to be normal. Control examination performed after six months suggested that attention and short-term memory had highly improved with no objective neuropathology.

Case-2: A 22-year-old woman at 12 weeks' gestation applied to the hospital with a history of severe nausea and vomiting, and was diagnosed as HE gravidarum and given anti-emetic therapy. She was followed up in the polyclinic for four weeks after which she had to be hospitalised because of uncontrollable nausea and vomiting. She received glucose, saline, anti-emetic containing therapy and parenteral nutrition throughout 7 days at the hospital. Oral nutrition was initiated and she

was discharged at the end of this period. Two weeks later, she was referred to our tertiary care hospital due to confusion, diplopia and neurological disorders, and was hospitalised. Physical examination revealed normotensive, tachycardia, multidirectional nystagmus and ataxia. According to the laboratory tests, alanine aminotransferase was 125 U/L (normal range, 0-55 U/L); aspartate transferase was 90 U/L (normal range, 5-34 U/L), while other laboratory parameters were found to be normal. In utero foetal death was detected by ultrasound. Cranial MRI showed hyperintensity areas in the posterior thalamus, pons and periaqueductal gray matter. With the diagnosis of WE, 100 mg of parenteral thiamine therapy was started. When major findings began to decline in four days, medical abortion was performed by misoprostol. The patient was discharged with persistent nystagmus after 30 days.

Discussion

WE was reported for the first time in 1881 by Carl Wernicke. In this syndrome, intracellular and extracellular oedema, glial cell proliferation, neuronal demyelination, and cellular degeneration may occur in the central nervous system (CNS), due to thiamine deficiency, which is the co-factor of enzymes such as transketolase, pyruvate dehydrogenase and alpha ketoglutarate dehydrogenase. Thus, thiamine deficiency causes increased accumulation of pyruvic acid and lactic acid leading to inadequate production of energy currency adenosine 5'-triphosphate (ATP) and the dependent Na+K+ATPase functions less and causes cytotoxic oedema. If changes persist, it may lead to cell death. Another mode of damage is excitotoxic cell damage due to accumulation of glutamate due to decreased activity of alpha ketoglutarate dehydrogenase.

Thiamine is a water-soluble vitamin. The recommended daily allowance is 1.1 mg, and the amount in the body is around 25-30 mg. During pregnancy, the requirement for thiamine increases in parallel to the foetal development, and therefore 1.5 mg thiamine is recommended to be taken with the daily diet.[2] Thiamine stored in the body usually lasts for around 18 days and inadequate oral intake for more than 3 weeks would increase the potential risk for developing thiamine deficiency.

HE gravidarum as a predisposing condition of WE was first reported in 1914. Throughout pregnancy and lactation periods, WE symptoms may be seen in the patients with gestational thyrotoxicosis and hyperthyroidism. Moreover, in the patients of hyperemesis gravidarum, uncontrollable vomiting, prolonged intravenous feeding, and thiamine-free glucose infusion therapy may lead to the development of WE.[3] Other factors like cancer, chemotherapy, alcoholics, acquired immune deficiency syndrome (AIDS) and the genetic defect becomes clinically important when the diet is deficient in thiamine.

Occasionally, visual deterioration may be the first sign of thiamine deficiency.[4] In the diagnosis of WE, the classic triad of symptoms, ocular abnormalities (93%), confusion (80%) and ataxia (76%) can be detected in 66% of the cases. Additional neurological findings are decrease in deep-tendon reflexes, loss of tonus and dysarthria. Some patients exhibit unexpected symptoms such as papillae oedema.[5] In our first case, visual deterioration was the first sign of thiamine deficiency. Papillitis due to thiamine deficiency may lead to progressive visual loss. In some cases, necrosis of the optic nerve cells and deterioration in the myelin structure can result in complete optic atrophy and blindness.[6]

WE is a clinical diagnosis and there is no specific routine laboratory test. MRI helps to exclude other diagnoses, such as vascular lesions and thrombophlebitis. To diagnose WE, MRI's sensitivity has been reported as 53%, while specificity as 93%.[7,8] The longest and shortest durations of vomiting until the development of WE have been reported as 17 weeks and 4 weeks respectively (median duration; 6 weeks).[9]

The level of thiamine does not always accurately reflect total vitamin B1 status, therefore it is not routinely tested.

In WE cases complicated with HE, preterm delivery, intrauterine growth retardation and miscarriage maybe experienced. Although with an efficient therapy we can achieve a healthy newborn. Spontaneous foetal loss rate is recognised as 37%, elective abortion rate is noted as 10%.[10] The differential diagnosis of WE includes intracranial haemorrhage, stroke, cerebral venous thrombosis, delirium, increased intracranial pressure, cerebral pathology, meningitis, pellagra, acute alcoholic and drug toxicity.

In the treatment of WE induced by hyperemesis, oral nutrition cannot be adequately managed because of severe vomiting and neurological symptoms. Thus, intravenous thiamine supplementation (100mg/day) is recommended in order to achieve rapid recovery.

Neurological symptoms reduce as soon as appropriate treatment is initiated. After thiamine replacement, 20% of patients may recover completely and 50% of ataxia improves completely. Defect in retentive memory and

learning typically generally persist. Ophthalmoplegia generally begins to improve within hours of thiamine treatment, otherwise, the diagnosis of WE should be suspected and re-evaluated. Besides, 15-20% of the hospitalised WE patients generally die of complications from infections or liver failure.

Conclusion

An alert eye should be kept at severe hyperemesis gravidarum for WE development. Prolonged glucose infusion therapy, oral or intravenous thiamine supplementation can be sufficient prophylaxis against dramatic foeto-maternal complications.

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