Wernicke's Encephalopathy Associated with Fetal Loss in a Patient with Severe Hyperemesis Gravidarum

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ABSTRACT

Wernicke's encephalopathy is an acute neurological condition caused by thiamine deficiency. It is a rare disorder which classically occurs in alcoholic patients due to recurrent vomiting and poor oral intake. When it occurs in non-alcoholics, it is often missed and consequent mortality and morbidity is high. Pregnancy complicated by hyperemesis gravidarum represents one important clinical setting in which Wernicke's encephalopathy may occur. We present the case of a 32-year old lady who presented in the 18th week of her third pregnancy with recent history of difficulty walking, visual symptoms, poor concentration and lethargy. She had suffered with hyperemesis gravidarum for the preceding 10 weeks. Obstetric ultrasound revealed a dead fetus of 16 weeks size. The patient's neurological features improved significantly after starting parenteral thiamine.

Key words: Hyperemesis gravidarum, Thiamine, Missed abortion, Wernicke's encephalopathy.

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Introduction

Wernicke's encephalopathy (WE) is a serious neurological disorder first described in 1881 by Dr Carl Wernicke, a Polish neurologist, as a triad of acute mental confusion, ataxia, and ophthalmoplegia, due to acute thiamine deficiency. It was first reported as a complication of hyperemesis gravidarum in 1914[(1)] and, subsequently, an increasing number of cases have been reported. The body stores of thiamine only last about three weeks and therefore WE may occur quite rapidly in patients with very poor oral intake or persistent vomiting.

WE is usually suspected in the setting of chronic alcoholism and may be missed when related to other conditions, associated with poor oral intake or malabsorption. It is a neurological emergency; the neurological manifestations are usually reversible if patients are treated promptly and adequately. Otherwise, it may progress to Korsakof's amnestic syndrome which is associated with severe memory impairment or result in death.

The fetal outcome in pregnancies complicated by thiamine deficiency has not been widely reported. We report a pregnant lady who presented with clinical features of WE and a missed abortion caused by intractable hyperemesis gravidarum. Early diagnosis and treatment led to a favorable maternal outcome.

Case report

A 32-year old housewife presented in the 18th week of her third pregnancy. Her previous two pregnancies were uneventful. She was transferred to King Hussein Medical Center (KHMC), from a district hospital where she was admitted a few days earlier for persistent and

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worsening hyperemesis gravidarum since the 8th week of her pregnancy. She had been treated with antiemetics and intravenous fluids containing dextrose solutions. Her condition deteriorated and she was transferred to KHMC for further management. She had no history of alcohol consumption or previous medical illnesses. She complained of sleepiness, lethargy, blurring of vision, diplopia and difficulty walking for the five days prior to admission to our hospital.

General examination was normal. On neurological examination, she was sleepy but easily arousable; she had poor attention and impaired short-term memory. Eye examination showed limited abduction bilaterally with gaze-evoked nystagmus. Visual acuity, color vision, pupillary reflexes and fundoscopy were normal.

Upper and lower limb examination showed mild proximal weakness, hyporeflexia and gait ataxia. Neurological examination was otherwise normal. An obstetric ultrasound was performed which revealed a 16 week fetus size with no cardiac motion; no gross anomaly was noted. A diagnosis of WE was strongly suspected, and she was immediately started on high-dose intravenous thiamine (200 mg tds) and magnesium (5g IV given once). Also, intravenous fluids containing dextrose were stopped.

Magnetic Resonance Imaging (MRI) of the brain showed symmetrical hyperintensity in the medial thalami and the area surrounding the third ventricle on Fluid-Attenuated Inversion Recovery (FLAIR) and Diffusion-Weighted Imaging (DWI) sequences (Fig 1, 2), findings were considered highly suggestive of WE, in the proper clinical setting.

Other laboratory investigations, including a complete blood count, clotting studies, biochemical profile, septic work-up and viral serology, were unremarkable. Cerebrospinal fluid examination showed a slightly raised protein of 74 mg/dl (Normal 15 - 45 mg/dl) but was otherwise normal.

Two days following the administration of thiamine, she had significant improvement in her oral intake, visual symptoms and gait. There was also improvement in her mood, alertness and memory. Her symptoms continued to improve over the next few days. Spontaneous abortion occurred on the fifth day of admission. No abnormalities were detected on gross examination of the fetus, placenta or the umbilical cord. Brain MRI was repeated approximately two weeks after treatment and showed definite improvement (Fig. 3). Within three weeks, she was almost back to normal, except for mild proximal weakness which improved over three months.

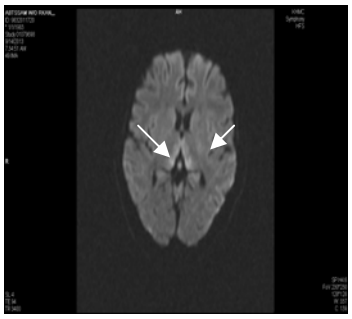

Fig. 1: (DWI sequence) on 14/9/2013

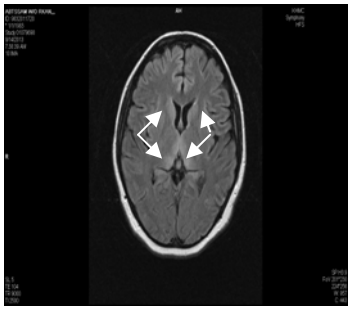

Fig. 2: (FLAIR sequence) on 14/9/2013

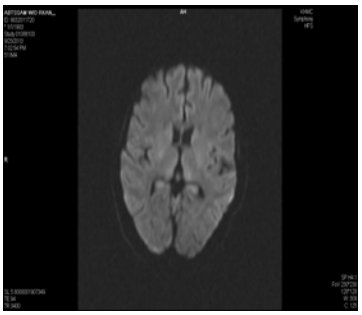

Fig. 3: DWI sequence after Rx (on 23/9/2013) showing significant improvement compared to Fig. 1

Discussion

WE is a syndrome characterized by the classic triad of confusion, ataxia, and ophthalmoplegia.[2] Wernicke-Korsak off syndrome usually results from deficiency of dietary thiamine, and typically occurs in chronic alcoholics.[3,4] It may also occur in conditions associated with poor oral intake and/or persistent vomiting such as gastrointestinal diseases, AIDS, and hyperemesis gravidarum.[5] A less common cause of

Wernicke-Korsakoff syndrome is an inborn genetic error of the utilization and metabolism of thiamine.[6] Thiamine is a co-factor for many enzymes such as transketolase, pyruvate dehydrogenase and alpha ketoglutarate dehydrogenase. Deficiency leads to inadequate production of adenosine 5-triphosphate (ATP) and consequently affects Na/K-ATPase-dependent functions causing cerebral cytotoxic oedema, and ultimately cell death.[6] Body stores of thiamine usually last around 18 days and, therefore, any condition causing persistent vomiting or severely reduced oral intake lasting 3-4 weeks may potentially lead to acute thiamine deficiency[7]. The early recognition of the clinical features of WE is crucial to the management of this condition. The diagnosis may be supported by brain magnetic resonance imaging, blood thiamine levels or reduced red cell transketolase levels but, the most practical method of establishing the diagnosis is the dramatic improvement which typically follows administration of high dose parenteral thiamine.[7]

Thiamine deficiency can be precipitated by three pregnancy-related conditions: hyperemesis gravidarum (0.1-0.5%), diabetic ketoacidosis and intravenous administration of glucose in the presence of chronically inadequate thiamine intake.[8] Thiamine deficiency may cause anorexia; this with the simultaneous increase in energy expenditure, may aggravate the condition in pregnancy.[9,10]

McGready *et al*.[11] observed that, despite the high incidence of thiamine deficiency in affected mothers, breast-milk thiamine concentrations remained within normal limits, suggesting preferential delivery of thiamine to the milk at the expense of the mother.

The daily requirement of thiamine in pregnancy increases by about one third (1.5 mg/day), due to the increased demand by the fetus and the hypermetabolic state of pregnancy. It is still unclear exactly what dose is required for full repletion of a deficient patient, and further research would be useful to clarify this question.[12]

The impact of maternal thiamine deficiency on the unborn baby and neonate is not well studied. Chiossi *et al*. observed an increase in the rate of fetal demise by 48% and only 28% of pregnant women had a resolution of symptoms.[13]

In our case WE was secondary to severe hyperemesis gravidarum and fetal loss was probably secondary to diverse metabolic derangements resulting from the intractable vomiting, including thiamine deficiency.[13]

Conclusion

Although WE is a rare disorder in pregnancy, a high index of suspicion for this condition should be maintained in any pregnant woman suffering with hyperemesis gravidarum who develops acute neurological symptoms. Early and adequate treatment is crucial to avoid maternal neurological damage and fetal loss.

Therefore our report would hopefully alert physicians managing pregnant women to these potential devastating complications of hyperemesis gravidarum.

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