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A rare complication of hyperemesis during pregnancy: Wernicke's encephalopathy

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Introduction

Wernicke's encephalopathy is a potentially reversible condition caused by thiamine deficiency. It is usually suspected in the setting of chronic alcoholism and might not be recognized when associated with other conditions. We describe a young pregnant woman with hyperemesis gravidarum, who on day 10 after her admission, presented with rapidly evolving ataxia, diplopia and confusion. Characteristic brain MRI findings and rapid response to thiamine suggested that she had Wernicke's encephalopathy, possibly due to vomiting and dextrose administration without thiamine supplements. A high index of suspicion is required, since delayed or lack of treatment may lead to high morbidity and mortality.

Case report

We report the case of a previously healthy pregnant woman, who was admitted to our hospital at 19 weeks' gestation with a four-day history of right sided upper abdominal pain, intractable vomiting and diminished appetite. Her past medical history was only significant for migraine without aura.

At admission, laboratory blood results showed haemoglobin of 9.5 g/dL (NR 12-16 g/dL), elevated levels in her liver function test results: γ-glutamyl transferase, 186 U/L (NR, < 49 U/L); alanine aminotransferase, 152 U/L (NR, < 55 U/L); and bilirubin, 0.3 mg/dL (NR < 0.3 mg/dL). The abdominal ultrasound revealed a considerable amount of sludge in the gall bladder, and therefore, she underwent a laparoscopic cholecystectomy. Over the next few days, she consumed hardly anything by mouth, continued to have intractable vomiting and received continuous intravenous dextrose administration without thiamine.

On day 10 after her admission, she developed an acute state of confusion, unsteadiness, and diplopia with oscillopsia. Upon neurological referral, we found a drowsy patient with a Glasgow Coma Scale of 12/15. She was oriented to place but not time. The neurological examination revealed multidirectional nystagmus, with limited upper gaze movement and severe ataxia.

The brain MRI performed the same day showed spontaneous hyperintensities on FLAIR and T2-weighed images in the posterior thalamus, the pons and the periaqueducal grey matter (Figs. 1A and 1B), with restricted diffusion in the posterior thalamus (Fig. 1C)

As the clinical signs and MRI findings were consistent with the diagnosis of Wernicke's encephalopathy, she was started on immediate intravenous thiamine replacement at doses of 300 mg/day. Thiamine levels in blood were not measured as this test is not carried out by the laboratory in the hospital.

Her condition improved gradually over the next few days, and the neurological examination done four days after showed major improvement, except for persistent mild ataxia which resolved over the next month.

Discussion

Wernicke's encephalopathy is a metabolic disorder due to Thiamine deficiency, first described by Carl Wernicke's in 1881. He first reported a trio of symptoms consisting of drowsiness, ophtalmoplegia and ataxia in three patients (two males with chronic alcoholism and one female with refractory vomiting after sulphuric acid ingestion). On autopsy, he

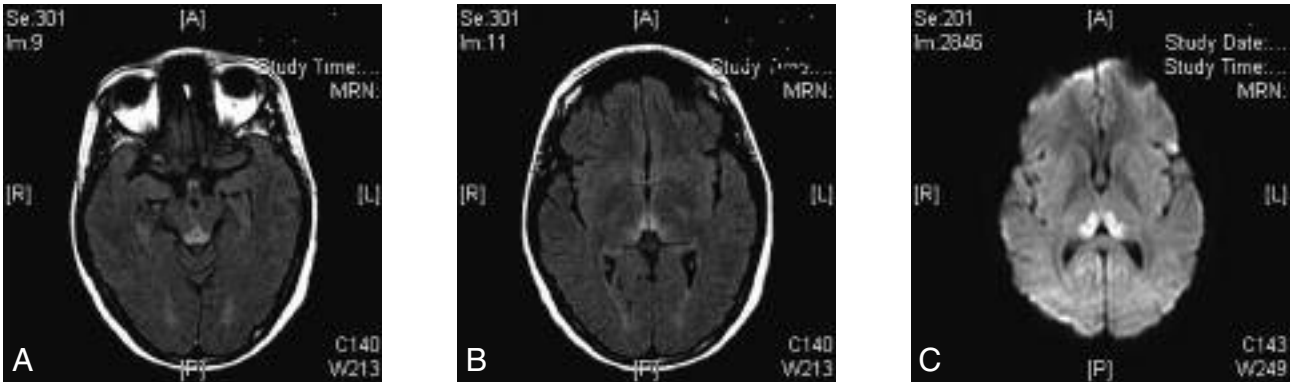

Fig. 1. — Axial T2 /FLAIR MRI images demonstrating spontaneous hyperintensities in the posterior thalamus, the pons and the periaqueducal grey matter (A and B). Diffusion-weighted axial MRI images showing restricted diffusion in the posterior thalamus (C).

detected punctuate haemorrhages affecting the grey matter around the third and fourth ventricles and aqueduct of Sylvius, and designated the term "polioencephalitis hemorrhagica superioris" (1).

In 1997, Caine et al. proposed an operational criterion for the recognition and diagnosis of Wernicke's encephalopathy accordingly; Wernicke's encephalopathy is recognized if there are two of the following four signs; (i) dietary deficiencies, (ii) oculomotor abnormalities, (iii) cerebellar dysfunction, and (iv) either an altered mental state or mild memory impairment (2).

Although most cases of Wernicke's encephalopathy seen in the western world today are related to chronic alcoholism, it is vital to recognise other rare causes of this condition, such as systemic diseases (malignancy, disseminated tuberculosis, acquired immunodeficiency syndrome (AIDS)), starvation (anorexia nervosa, prisoners of war, schizophrenia, terminally ill cancer patients), iatrogenic (refeeding after starvation, chronic haemodialysis), and persistent emesis such as hyperemesis gravidarum. The prevalence of Wernicke's encephalopathy in a non-alcoholic patient varies from 0.04% to 0.13% (3).

Wernicke's encephalopathy in a patient with hyperemesis gravidarum was first described by Sheehan in 1939 (4). To our knowledge, only 49 cases of Wernicke's encephalopathy during pregnancy have so far been reported in the literature (5).

The mechanism by which thiamine deficiency causes the focal neuropathology lesions found in Wernicke's encephalopathy might be multiple (6). Thiamine is an important co-enzyme for three critical enzymes in the Kreb's and pentose phosphate cycle: transketolase, ketoglutarate dehydrogenase, and pyruvate dehydrogenase complex. Deficiency of thiamine and hence deficiency of these enzymes result in focal lactic acidosis, cerebral energy impairment, depolarization of neurons due to n-methyl-D-aspartate receptor mediated excitotoxicity. Ultimately, it results in alteration of blood brain barrier, generation of free radical, prompting cell death by necrosis and apoptosis (6).

The body has approximately 18 days of thiamine storage. It is well understood that thiamine requirements are increased during pregnancy, and even more by the impaired absorption due to hyperemesis gravidarum (7). Thiamine dependence is also increased in conditions with high metabolic rates and high glucose intake, and therefore its depletion due to reduced intake as well as IV dextrose administration results in thiamine deficiency and Wernicke's encephalopathy (8, 9).

The treatment for Wernicke's Encephalopathy includes high doses of thiamine, 500 mg per day, given eighth hourly for two days followed by 250 mg per day once daily until the patient tolerates oral thiamine (11).

Our patient presented with the classical clinical triad following intractable vomiting and dextrose administration without thiamine supplementation. MRI imaging also detected sensitive neurological changes, raising the suspicion of an acute stage of thiamine deficiency. These findings were important for prompt diagnosis and treatment of our patient's condition when clinical signs began to emerge. Indeed there are reports of the usefulness of MRI imaging in diagnosing cases of Wernicke's encephalopathy (10).

Wernicke's encephalopathy should be suspected in any nutritionally compromised patient who shows altered mental status before manifestation of the classical triad as, if left untreated, it could lead to evere irreversible and persistent neurological sequela or death.

We would like to emphasize the importance of prompt thiamine supplementation in pregnant women with prolonged vomiting in pregnancy, especially before starting intravenous or parenteral nutrition.

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