

# Loss of Vision: A Rare Presentation In Hyperemesis Gravidarum Induced Wernicke's Encephalopathy

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## Abstract

Wernicke's encephalopathy (WE) is a potentially fatal but readily reversible medical emergency caused by thiamine deficiency. WE is most commonly associated with heavy alcohol consumption, but is also seen in other clinical settings such as Hyperemesis Gravidarum (HG), starvation, and prolonged intravenous feeding. After Sheehan's first description of WE following HG there are few case reports of similar etiology from various parts of the world [1,2,3,4]. WE is popularly known and taught as the clinical triad of ophthalmoplegia, confusion and ataxia. We discuss a pregnant woman with HG presenting with visual deterioration and her optic fundi showing optic disc edema on right side and retinal hemorrhage on left side. Its a rare initial presentation of WE.

## INTRODUCTION

Wernicke's encephalopathy (WE) is a potentially fatal but readily reversible medical emergency caused by thiamine deficiency. WE is most commonly associated with heavy alcohol consumption, but is also seen in other clinical settings such as Hyperemesis Gravidarum (HG), starvation, and prolonged intravenous feeding. After Sheehan's first description of WE following HG there are few case reports of similar etiology from various parts of the world [1,2,3,4]. WE is popularly known and taught as the clinical triad of ophthalmoplegia, confusion and ataxia.

We discuss a pregnant woman with HG presenting with visual deterioration and her optic fundi showing optic disc edema on right side and retinal hemorrhage on left side. Its a rare initial presentation of WE.

## CASE REPORT

A 26 years old primigravida, at 20 weeks of gestation was admitted because of rapidly deteriorating visual loss of 2 days duration. She started vomiting during the 8<sup>th</sup> week of gestation for which she was admitted twice and treated with anti-emetics and intravenous fluids. She continued to have persistent vomiting and complained of general weakness. Two days earlier to admission to our hospital she noticed deterioration of vision in both eyes. She did not have

headache or loss of consciousness. Her antenatal record was unremarkable except for HG. Her pulse was 100/mt; BP 90/60 mmHg. Fetal heart sound was absent and antenatal ultrasonogram showed single non vital fetus of 16 week gestation. Medical termination of pregnancy was planned.

On day 3 of admission, she was referred to the neurology service. She was confused, drowsy, but followed simple commands. Her pupils were bilaterally equal and reactive. She had bilateral lateral rectus palsy with gaze evoked nystagmus in horizontal direction and her vertical eye movements were normal. She had normal motor power in all 4 limbs with sluggish muscle stretch reflex in lower limbs and plantars were flexors. She had lower limb ataxia. There was no neck stiffness. Her past history was unremarkable. She was not on any medication. She was neither a smoker nor an alcohol consumer. There was no pain on eye movements. Visual acuity was 6/36 in Rt and 6/18 in Lt. Her visual field was normal on confrontation. Optic Fundi showed optic disc edema on right side and retinal hemorrhage on left side.

The following investigations were normal or negative; full blood count, sedimentation rate, anti- nuclear antibody screening, HbsAg, serology tests for syphilis and HIV, blood sugar, urea, creatinine, Sr calcium , Phosphate., Bilirubin,

AG ratio, INR and Gamma GT. She had hypokalaemia (2.8mEq/L), mildly elevated SGOT and SGPT (175 IU and 185 IU respectively). No proteinuria and glycosuria was present in the urine analysis.

Clinical diagnosis of cerebral venous thrombosis was considered in view of bilateral lateral rectus palsy and optic disc edema with retinal hemorrhage. Her MRI brain (T2WI and Flair) showed symmetrical hyperintense lesions in the medial thalamus and periaqueductal gray matter in midbrain. Given the history of HG and the typical MRI findings the revised diagnosis was WE. Intra uterine death was confirmed by a repeat ultrasonogram on day 2. In the absence of spontaneous contraction, abortion was induced on day 4 by means of extra amniotic prostaglandin E2. The fetus and placenta were macroscopically normal.

The patient was treated with 500mg/day of IV thiamine for initial 2 days then 300mg/day of for next 3 days. She made rapid improvement in her vision and eye movements. Her Optic disc and eye movements were normal on Day 7 but had partial improvement in ataxia. Nerve conduction studies done at the end of 1<sup>st</sup> week showed normal conduction velocity, distal latency and amplitude of median, ulnar, common peroneal and sural nerves.

### **DISCUSSION**

Wernicke's encephalopathy (WE) is an acute neurologic disorder resulting from thiamine (vitamin B1) deficiency. WE was first described by Carl Wernicke [5] in 1881 as "superior acute hemorrhagic polioencephalitis" in two men with alcoholism and in a woman affected by pyloric stenosis, whereas the association of WE with thiamine deficiency was first suspected in the 1940s [6]. The exact prevalence and incidence of WE are unknown, but necropsy studies have revealed incidence rates ranging from 0.5% over a 5-year period in Norway to 2.8% over a 9-year period in Australia [7, 8].

Traditionally, the clinical diagnosis of WE rests on the classical triad of ophthalmoplegia, altered consciousness, and ataxia, already described by Wernicke [5] in his original article. However ocular signs such as nystagmus, bilateral lateral rectus palsies, and conjugate gaze palsies are common findings rather than ophthalmoplegia [9]. In a necropsy study of 131 patients with WE, it was found that only 16% of them present with the clinical triad while 19% had no documented clinical signs [7]. In view of the poor diagnostic performance of the classical triad, new classification criteria have been proposed. These criteria require two of four items including

dietary deficiencies, oculomotor abnormalities, cerebellar dysfunction, and an altered mental state or mild memory impairment [10]. Though our patient had the classic triad, her initial presentation as rapidly progressive visual loss with optic disc edema is unusual.

In 1941, George Black first documented a case of WE with retinal hemorrhage without mention on optic disc edema. He believed that the fundus picture of large darkish hemorrhages splashed around the disc to be probably fairly characteristic of WE and with necropsy finding he stated that these fundus lesions illustrate the close correspondence between the retina and brain [11]. Papilloedema is recorded very infrequently in literature. [12, 13, 4]. In an analysis of ocular signs in WE performed on a series of 52 Japanese prisoners-of-war, only two cases (4%) were found to have papilloedema [14]. Retinal haemorrhages without papilloedema are probably a more frequent manifestation, but in an exhaustive study of 245 patients in Boston, small retinal haemorrhages were an associated finding in only six cases (2%). No cases were seen with papilloedema or other abnormalities of the optic disc [15]. Disc hyperaemia and retinal haemorrhages are generally considered to be secondary to optic disc oedema. The most straightforward explanation for such nerve fibre swelling in the present context would be to postulate a WE associated optic neuritis or neuropathy, analogous to the nutritional retrobulbar neuropathies such as those reported in pellagra and associated with tobacco [16]. Mumford CJ speculated an alternative theory regarding the few cases of WE where papilloedema and/or retinal haemorrhages are seen. These findings might result from the occurrence of the typical neuropathological features of WE characterized by necrosis of both nerve cells and myelinated structures, and subsequent oedema, within the optic nerves themselves [17]. Cook et al reported bilateral visual disturbances with optic-disc oedema and retinal haemorrhages as the presenting features of Wernicke's encephalopathy in a 11 year old boy [13]. Causes for visual disturbances and raised intra cranial tension are many in pregnancy. The clinician should be alert in suspecting WE in all its atypical presentations in HG such as loss of vision, loss of equilibrium and fetal loss.

More than 40 cases of Wernicke's encephalopathy associated with hyperemesis gravidarum have been described. Recent case studies also reveal a vulnerability in patients with thiamine deficiency secondary to chemotherapy-induced hyperemesis, Crohn's disease, AIDS, self-induced starvation, bariatric surgery and long-term

parenteral nutrition[18]. Any individual who is lacking a source of thiamine for more than a few weeks is at increased risk, particularly if he or she receives glucose-containing intra venous fluids or a glucose-rich diet. In HD, fetal loss - because it often precedes overt focal signs in the mother- might be the first sign [19]. With the developing fetus being particularly at risk, fetal loss is not uncommon. In our case WE was secondary to severe HG and fetal loss was probably secondary to thiamine deficiency as no other definite cause could be identified. Fetal brain autopsy was not done .

Measurement of thiamine level in blood is not a prerequisite for the diagnosis of WE. Interestingly, serum thiamine level was normal in this case. By the time the report was available on 6<sup>th</sup> day, she made remarkable recovery in her vision and lateral rectus weakness. Intracellular thiamine level is usually a more accurate marker of thiamine deficiency, measured as erythrocyte thiamine diphosphate by high pressure liquid chromatography, and is often abnormal in cases of WE, even when the serum thiamine level is normal[20]. MRI findings that are strongly suggestive of WE include symmetrically increased signal intensity on FLAIR and T2-weighted images in the paraventricular areas of the thalamus, hypothalamus, mamillary bodies, periaqueductal midbrain, or cerebellum[21]. These findings may be explained by the maintenance of cellular osmotic gradients that are strictly related to the concentration of thiamine levels in these areas. The MRI of brain has high (93%) specificity and moderate (53%) sensitivity [22] in the diagnosis of WE. Zhong et al analyzed the serial MRI findings in 6 non-alcoholic patients with WE and concluded that patients without coma show only periventricular damage. With further alteration in consciousness there was involvement of the medial thalami and capita of caudate nuclei. WE is remediable when there is involvement of only the peri-aqueductal regions, medial thalami and caudate. Involvement of the cortical regions indicates irreversible damage and poor prognosis [23]. In our case MRI helped to rule out common causes of raised ICT in pregnancy and suggested the possibility of WE by showing symmetrically increased signal intensity on FLAIR and T2-weighted images in the medial thalamus and periaqueductal midbrain.

The cornerstone of treatment remains the timely administration of thiamine. But how much and how long is an answered question. The traditional recommendation is a parenteral dosage of 100 mg of thiamine per day [24]. No randomized, controlled, clinical trial has tested this regimen. This dosage has been contested by several British authors

who recommend a dosage of 500 mg, although little evidence is available to support or refute this regimen [25]. These authors hypothesize that very high doses are necessary to obtain optimal passive diffusion of thiamine across the blood-brain barrier, and they cite examples of failure of cure and even death with lower-dose thiamine to support higher dosing. They recommend 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. Subsequently oral thiamine 100 mg twice daily for a minimum of at least three months may be prescribed. Our patient was treated with 500mg/day of IV thiamine for initial 2 days then 300mg/day of for next 3 days. She made rapid improvement in her vision and eye movements. Her optic disc and eye movements were normal on day 7 of thiamine replacement but had partial improvement in ataxia.

Wernicke's encephalopathy is an often unrecognized disease of nutritional deficiency. Though most prevalent in alcoholics, WE may occur in anyone who develops a nutritional deficiency of thiamine. The classic triad of mental status changes, ophthalmoplegia, and gait ataxia is often absent. Recognition of WE in its typical and atypical presentation should prompt treatment. Treatment demands immediate intravenous administration of thiamine, although the exact dosage regimen is unclear. Early recognition and rapid treatment will help prevent the devastating consequences of a treatable disease.

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