Wernicke’s Encephalopathy with Visual Loss in a Patient with Hyperemesis Gravidarum

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Abstract

Objective: We describe a case of Wernicke’s encephalopathy associated with visual loss that was caused by hyperemesis gravidarum.

Methods: A 25 year old lady in her 20th week of pregnancy consulted us. She had history of nausea and vomiting for 3 months with resultant weight loss. She now presented with sub-acute onset of visual loss in both her eyes, and gait disturbance with unsteadiness. Upon ophthalmologic examination she was found to have a visual acuity of 6/60 in both eyes; abduction restriction, nystagmus and retinal hemorrhages and macular oedema in both eyes. She also had truncal, stance and gait ataxia.

Results: She was treated with parenteral thiamine and her visual loss reversed and her ataxia improved dramatically. Magnetic resonance imaging (mRI) brain with diffusion weighted imaging showed findings consistent with Wernicke’s Encephalopathy.

Conclusion: Wernicke’s Encephalopathy can occur in many hitherto under-recognised clinical scenarios associated with inadequate oral intake like hyperemesis gravidarum, after gastric bypass surgeries and those on total parenteral nutrition. Visual loss is increasingly being recognized as the additional, reversible feature of Wernicke’s Encephalopathy. The changes that occur on mRI brain, especially on the diffusion weighted images, are characteristic and considered diagnostic of Wernicke’s Encephalopathy.

Introduction

Wernicke’s encephalopathy is a neurological emergency caused due to thiamine deficiency. Though it is usually seen in chronic alcoholics, it is a common condition in many other clinical settings including malnutrition, hyperemesis gravidarum, cancer and gastric surgeries. The practice of administering glucose containing infusions in hospitals could precipitate Wernicke’s disease in a previously unaffected patient or cause worsening of an early form of the disease, as described in this patient. The diagnosis is hugely clinical and unless sought for specifically is often missed, thereby a potentially reversible condition could lead on to stupor, coma, and death. We present this case to highlight the clinical presentation of Wernicke’s disease with visual disturbance as a manifestation, hitherto under-recognised.

Case Report

A 25 year old lady in her 20th week of pregnancy has had nausea and vomiting for the past three months. She has noticed a weight loss of over 10% of her body weight over the last two months. She developed sudden onset diminution of vision in both her eyes, which progressively worsened over the next two days till she could only count fingers. She was admitted in the hospital for the same complaints and was administered intravenous fluids as she waited for a consult with her obstetrician. About six hours after admission, she noticed that she was swaying back when she sat up and could not stand without swaying. She also noticed double vision. She was referred to our institute at this point.

Clinical examination revealed that she was pale, conscious, oriented to time, place; her higher functions were intact. Her visual acuity was limited to finger counting at the distance of 1 meter. Fundus examination showed bilateral retinal hemorrhages and macular edema (Figures 1 and 2). She had bilateral abduction restriction and horizontal end gaze nystagmus. She also had in-coordination, stance, and gait ataxia. Investigations revealed an hemoglobin level of 8.6g/dl, normal platelet counts. Her electrolytes were normal with serum sodium of 138 m Eq/L and serum potassium of 3.7 m Eq/L. Ultra-sonogram confirmed a live single intrauterine foetus with good cardiac activity.

We obtained a neurology consult. With nystagmus and ataxia in a patient with inadequate intake, a provisional diagnosis of Wernicke’s encephalopathy was made in this case. As serum thiamine levels are not routinely available, she was started on parenteral thiamine. The patient showed dramatic recovery: with the first dose of 100 mg of thiamine, her visual acuity improved to 6/6 in the first 24 hours and her nystagmus resolved completely. In the following week of treatment, her in-coordination improved by 60-70 %, nausea improved, and she has resumed feeding orally. A repeat fundus examination showed complete resolution of the retinal hemorrhages and macular oedema (Figures 3 and 4).

MRI Brain was done on the third day after admission and the T1 and T2 images were reported as normal. Diffusion weighted images were obtained the following day to reveal hyper-intensities in the dorso-medial nucleus of the thalamus, an area frequently involved in Wernicke’s encephalopathy. These hyper-intensities were suppressed on the ADC (apparent diffusion coefficient), a picture consistent with reversible cytotoxic oedema in the area affected (Figures 5 and 6).
Discussion

Wernicke’s encephalopathy is caused due to thiamine deficiency and is usually seen in chronic alcoholics and is also seen in many cases with inadequate oral intake like hyperemesis, anorexia nervosa, gastric bypass surgeries, hemodialysis and total parenteral nutrition.

The daily requirement of thiamine is around 1-1.2 mg/day and is mainly supplied by dietary sources. In pregnancy the demand for thiamine increases. The thiamine stores in the body usually last for around 18 days. So any patient with inadequate oral intake for more than three weeks would be at potential risk for developing thiamine deficiency. Thiamine is an essential cofactor in the carbohydrate metabolism. It is required in the following reactions:

- Pyruvate dehydrogenase
- Alpha-keto glutarate dehydrogenase

Transketolase of pentose phosphate pathway

So non availability of thiamine causes increased accumulation of substrates like pyruvic acid and lactic acid. This is coupled with the inadequate production of the energy currency ATP due to impaired carbohydrate metabolism. The ATP dependant Na+ K+ ATP ase functions less and causes cytotoxic odema along with the accumulating lactic and pyruvic acid. If these changes are persistent, it leads on to cell death. Another suggested mode of damage is the excitotoxic cell damage mediated through the accumulation of glutamate due to decreased activity of alpha keto glutarate dehydrogenase.

Carbohydrate loading, either oral or intravenous may precipitate Wernicke’s encephalopathy through the mechanism elucidated, thereby making it absolutely essential to consider thiamine replacement before administering glucose containing infusion to patients, who are chronically malnourished.

The areas of the brain which are particularly susceptible
to these changes happen to be the periventricular regions surrounding the third ventricle, aqueduct and fourth ventricle, namely dorsomedian nucleus of the thalamus, mamillary body, hypothalamus, superior part of cerebellar vermis.2

The clinical manifestations of Wernicke’s encephalopathy includes confusion, ataxia and ophthalmoplegia. The clinical manifestations correlate with the areas usually affected. The classical clinical triad is seen only in 15-30% of patients.2 The other manifestations include autonomic disturbances, hypothermia nausea etc. More recently there are increasing reports about visual disturbances and manifestations like retinal hemorrhages, macular oedema, papilledema and papillitis.3 Thiamine might have a role in preserving vascular integrity, the loss of which can lead to retinal hemorrhages. This can be supported by the recent studies done in the field of experimental diabetic retinopathy by the use of benfotiamine, a lipid-soluble, thiamine derivative, to prevent diabetic retinopathy. Benfotiamine can inhibit three pathways that are implicated in the pathogenesis of hyperglycemia-induced vascular damage: the hexosamine pathway, the advanced glycation end product (AGE) formation pathway and the diacylglycerol (DAG)-protein kinase C (PKC) pathway. These pathways are activated by increased availability of the glycolytic metabolites glyceraldehyde-3-phosphate and fructose-6-phosphate, as well as by hyperglycemia-associated, NF-kappa B activation, and by glyceraldehyde-3-phosphate and fructose-6-phosphate, as well activated by increased availability of the glycolytic metabolites glyceraldehyde-3-phosphate and fructose-6-phosphate, as well as by hyperglycemia-associated, NF-kappa B activation, and by activating the pentose phosphate pathway enzyme transketolase, converts glyceraldehyde-3-phosphate and fructose-6-phosphate into pentose-5-phosphates and other sugars. In retinas of diabetic animals, benfotiamine treatment inhibited these three pathways, inhibited NF-kappa B activation by activating transketolase, and thus prevented experimental diabetic retinopathy. Therefore, these above-mentioned report, suggest that thiamine deficiency causes a decrease in transketolase activity, and that this may cause vascular damage, all of which can give rise to retinal hemorrhage.4

Wernicke's encephalopathy is essentially a clinical diagnosis. Clinical improvement to therapy is considered diagnostic. The diagnosis can be aided by demonstrating decreased serum thiamine levels. Another technique is to measure the erythrocyte transketolase activity before and after administering thiamine. If an increase of 25 % of the enzyme activity is noted, then it is suggestive of thiamine deficiency. Neither of these tests are fool proof nor standardized in our laboratories. Even clinical suspicion of this disease warrants administration of thiamine. 50-100 mg of thiamine administered intravenously and 100mg of thiamine intramuscularly thereafter till the patient resumes adequate oral intake and 10mg of thiamine PO qd thereafter.2

Magnetic resonance imaging of the brain may reveal hyperintensities in T2 weighted images in the areas noted above. Diffusion weighted imaging is increasingly being used in the radiological diagnosis of Wernicke's encephalopathy. It is considered to be more sensitive at picking up a greater number of patients in whom T2 weighted images appear normal. Diffusion weighted imaging shows images which appear as hyperintense lesions in diffusion images, and are suppressed on the apparent diffusion co efficient (ADC) images. This pattern is suggestive of cytotoxic oedema. The lesions thus demonstrated characteristically disappear with administration of thiamine. This technique is increasing being used to document the diagnosis of Wernicke’s encephalopathy especially in comatose patients in whom the ocular findings or ataxia may be difficult to demonstrate.5 Thus, a low threshold for clinical suspicion of thiamine deficiency, recognition of atypical clinical presentations including visual loss due to macular oedema and retinal hemorrhages, adequate utilization of advances in magnetic resonance imaging and prompt administration of therapy can result in extremely gratifying results in this potentially reversible neurological emergency.

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References