Commentary

Thiamine (vitamin B1) is an essential coenzyme for mitochondrial oxidative decarboxylation serving as a cofactor for pyruvate and 2-oxoglutarate dehydrogenase complexes, required for the mitochondrial synthesis of adenosine triphosphate (ATP), and for transketolase, a cytosolic enzyme involved in the pentose-phosphate cycle that plays an important role in maintaining cell redox status.[1] Furthermore, thiamine diphosphate, also known as thiamine pyrophosphate is needed in the cell membrane to sustain osmotic gradients.[2] Therefore, thiamine deficiency may cause cellular swelling and local disruption of the blood-brain barrier.[2] In fact, the interrelation between thiamine and osmolality explains the findings showed in this issue of the Journal of Neurosciences in Rural Practice by Sutamnartpong and colleagues:[3] Wernicke's encephalopathy (WE) and central pontinemyelinolysis (CPM).

WE and CPM are two life-threatening metabolic encephalopathies, which have a high rate of under-diagnosis due to the relatively variable clinical presentations.[4]

Based upon animal studies, encephalopathy will occur when brain thiamine stores fall below 20% of normal levels.[5] In these cases, thiamine-deficient cell membranes are unable to maintain osmotic gradients resulting in the swelling of intracellular and extracellular spaces with cytotoxic edema and vasogenic edema.[2,6] Therefore, pathological features are edema, spongy degeneration of the neuropil, swelling of capillary endothelial cells and extravasation of erythrocytes.[2]

Thiamine is absorbed in the jejunum and ileum by an active, carrier-mediated, and rate-limited process, but at higher concentrations, the uptake is by passive diffusion.[7] The recommended daily allowance for thiamine is only 1.1-1.2 mg, although in pregnancy the daily requirement is increased (up to 1.5 mg) because of the increased demand of thiamine for the fetus and the hypermetabolic state of pregnancy.[8] In addition, hyperemesis gravidarum is another major cause of thiamine deficiency. Furthermore, chronic alcohol abuse leads to thiamine deficiency, and inhibition in intestinal thiamine absorption plays a role in causing this deficiency. This inhibition is associated with a marked decrease in the level of expression of thiamine transporter–1 (THTR-1).[7]

In this very interesting case report,[3] the patient had the classic triad of WE which includes ocular abnormalities (nystagmus, ophthalmoplegia, papillary abnormalities, optic neuropathy), ataxic gait, and mental status changes.[7,8] Nonetheless, diagnosis can be difficult as presentation may be atypical,[8] so a high index of suspicion is needed in high-risk patient populations.

Serum and red blood thiamine levels represent just a small portion of the total body thiamine content and are not reliable indicators of thiamine status.[1,7] Notwithstanding, in clinical practice routine tests are not usually recommended. In this respect, Sutamnartpong *et al*.,[3] demonstrated that thiamine supplementation even without confirmatory tests of thiamine deficiency, results in resolution of clinical symptoms.

Nevertheless, the 2010 European Federation National Societies (EFNS) guidelines for diagnosis and therapy of WE recommend that a blood sample should be sent for high-performance liquid chromatography (HPLC) analysis, prior to parenteral thiamine administration.[9]

The EFNS guidelines recommend magnetic resonance imaging (MRI) to support the diagnosis of WE

(sensitivity 53% and specificity 93%).[10] The most frequently used diagnostic images are Fluid-Attenuated Inversion Recovery (FLAIR) and T2-weighted images.[6,11] Symmetrical hyperintense changes indicative of brain edema are typically seen in tissues surrounding the thalami (as in this clinical case), mamillary bodies, tectal plate and periaqueductal area, whereas signal intensity alterations in the cerebellum, including the vermis, cranial nerve nuclei, red nuclei, dentate nuclei, caudate nuclei, and cerebral cortex, represent atypical MR imaging find ings.[4,6,8,10,12] In CPM, MRI usually shows a centrally located lesion in the pons and extrapontine structures such as the cerebral white matter, thalamus, and basal ganglia may be involved with hyperintense lesions on T2-weighted and FLAIR imaging.[11]

Regarding thiamine supplementation in WE and CPM, there is no evidence to recommend the best dosage, route of administration and treatment time.[1] Although it has been the practice to administer thiamine parenterally in dosages of 100 mg three times a day, more recent guidelines recommend that thiamine should be given intravenously 200 mg three times daily.[1,7] In all cases, intravenous thiamine supplementation must be given before feeding, and standard diet should be started only after thiamine administration to avoid a serious complication: The *refeeding syndrome*. Meanwhile, alcoholic patients with WE and CPM may need doses as high as 500 mg three times daily.[1,7]

In conclusion, the current case report[3] is helpful to remind that WE and CPM are two potential life-threatening complications in hyperemesis gravidarum. A high index of suspicion should result in immediate high-dose intravenous thiamine without waiting for a laboratory confirmation of thiamine deficiency.

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