

# A Rare Case of Wernicke's Encephalopathy and Dry Beri-beri Complicating Hyperemesis Gravidarum.

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## ABSTRACT

Hyperemesis gravidarum occurs in approximately 0.3-2.0% of pregnancies. We present a rare case of Wernicke's encephalopathy and dry beriberi as a complication of hyperemesis gravidarum. A 23-year-old female, at 19 weeks gestation, presented with persistent vomiting since early pregnancy and feeling generally weak. Transabdominal ultrasound on presentation confirmed a non-viable foetus which was surgically removed. Throughout admission, she was noted to have confusion lasting a few days, horizontal nystagmus and progressive weakness with peripheral neuropathy of bilateral lower limbs. Her CT brain and lumbar puncture was normal. Nerve conduction studies was done, and coupled with her neurological findings, conclusion of thiamine deficiency was made. She was treated with thiamine and with rehabilitation she has currently made significant improvement. Thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi in patients with hyperemesis gravidarum is rare.

**Key words:** Wernicke encephalopathy, Beriberi, thiamine deficiency, hyperemesis gravidarum

## INTRODUCTION

Hyperemesis gravidarum is a complex condition with a multifactorial aetiology characterized by severe intractable nausea and vomiting.<sup>1</sup> Hyperemesis gravidarum occurs in approximately 0.3-2.0% of pregnancies.<sup>1</sup> Wernicke's encephalopathy is a well known sequelae of thiamine deficiency which can occur in hyperemesis gravidarum.<sup>2</sup> It is characterised by the classic triad of encephalopathy,

ophthalmoplegia and ataxia. In dry beriberi there is usually symmetric, non-specific polyneuropathy with myelin degeneration and disruption of motor, sensory and reflex arc which occurs with thiamine deficiency. We report a rare case of Wernicke's encephalopathy and dry beriberi as a complication of hyperemesis gravidarum. This patient was treated with thiamine, and with rehabilitation she has had significant improvement of her neurological symptoms.

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## CASE REPORT

A 23-year-old female, at 19 weeks gestation, presented with persistent vomiting up to 10

times a day since early pregnancy and generalised weakness. She had poor appetite and reduced oral intake for over a month prior to presentation. She experienced significant weight loss of at least 5 kilograms. There were no other significant symptoms. She had been attending the emergency department and her local clinic a few times, and was treated for urinary tract infection once and had been given intravenous hydration. Premorbidly, she had a complete miscarriage 2 years previously. She did not take any traditional or over the counter medications. She did not consume alcohol.

On examination, there was evidence of dehydration with dry mucous membranes. Uterus was palpable corresponding to 18 weeks of gestation. Initial haematological investigations showed increased urea (16.7 mmol/L) and creatinine (180 µmol/L); low sodium (129 mmol/L), potassium (2.0 mmol/L) and magnesium (0.53 mmol/L); abnormal liver function tests (ALP: 113 U/L, AST:217 U/L, ALT: 367 U/L); and metabolic alkalosis on venous blood gas. Urine dipstick showed ketone:4+, urobilinogen: 4+, bilirubin: 1+, leukocytes: 3+ and nitrate: negative. Thyroid function test was normal. B12 and folate levels were normal as well. Transabdominal ultrasonography showed single non viable foetus, in which foetal heart activity was not seen.

She was admitted for intravenous hydration, with magnesium and potassium replacement. A course of amoxicillin-clavulanate was commenced. Suction and curettage was done for removal of products of conception. Despite these treatments, and also an improvement in her vomiting, her weakness persisted. She was unable to walk and also had reduced sensation of lower limbs bilaterally which has progressed for a few days since admission. She also had intermittent confusion which lasted a few days. On neurological examination, her Glasgow Coma Scale was

full. Examination of lower limbs showed normal tone, power  $\frac{3}{5}$  at the hip,  $\frac{2}{5}$  at the knees and  $\frac{1}{5}$  of both dorsi and plantar flexion. Reflexes were absent throughout both lower limbs, and absent sensation of all modalities in a stocking distribution up to level of thighs. She was unable to stand. Upper limbs examination showed normal tone, power of  $\frac{4}{5}$ , with absent reflexes and normal sensation. There was presence of horizontal nystagmus, and past pointing bilaterally.

At that time, potassium level remained low at 3.0 mmol/L. Other renal profile and liver function tests had normalised. Magnesium had also normalised after replacement. Creatinine kinase was normal. Her potassium was immediately replaced, however her neurological symptoms persisted despite normalisation.

She had a computed tomography of the brain which was normal. Lumbar puncture showed normal protein, glucose, no organism on gram stain, and no evidence of malignancy or infection. Histopathology results from suction and curettage confirmed products of conception, no malignancy and no hydropic changes were noted. Nerve conduction study (NCS) showed evidence of predominantly sensory with mild motor axonal polyneuropathy involving both upper and lower limbs. There was no evidence suggestive of demyelination and F waves were normal. A provisional diagnosis of thiamine deficiency was made in the context of recurrent vomiting throughout pregnancy, poor oral intake, memory impairment with mild horizontal nystagmus and NCS findings. Thiamine level in whole blood was sent with expectant results in 4 weeks.

A 5 day course of parenteral multivitamin replacement was immediately commenced, followed by oral thiamine supplementation. There were no further episodes of confusion after replacement. Subsequently

her test result revealed a low thiamine level (52nmol/L (66-200nmol/L)). A final diagnosis of Wernicke's encephalopathy and dry beriberi secondary to hyperemesis gravidarum was made.

Rehabilitation was initiated with involvement of the physiotherapist and occupational therapist teams. After 4 weeks of rehabilitation she was able to stand, with gradual return of reflexes and sensation. She was transferred to a specialist rehabilitation unit for continuation of rehab.

## DISCUSSION

The above case describes a pregnant patient with thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi. Although it is a recognised complication of hyperemesis gravidarum, it is rare to present with both central and peripheral neurological symptomatology. Improvements in health systems and care delivery in Malaysia, with a great emphasis on maternal and child wellness, such overt manifestations of thiamine deficiency is rarely seen in pregnant mothers in routine day to day practice.

Thiamine (vitamin B1) is a micronutrient that is easily available in the diet through foods such as rice, grains and lean meat.<sup>3</sup> Widespread consumption of refined foods such as polished rice, white sugar and white flour could predispose to reduced dietary availability of thiamine as they contain very little amounts.<sup>3</sup> Once thiamine is absorbed from the gut it undergoes phosphorylation to produce thiamine pyrophosphate (TPP) which is a functionally active coenzyme of the vitamin.<sup>3</sup> Among the major functions of TPP is to regulate oxidative decarboxylation of alpha-ketoacids to produce adenosine triphosphate (ATP), acts as a cofactor in the pentose phosphate pathway and in a manner that has not yet been fully determined maintains neural

membranes and normal nerve conduction (mainly peripheral nerves).<sup>3</sup>

Thiamine deficiency has been well known to cause multi-system manifestations including to the nervous system, cardiac system, gastrointestinal system and vision.<sup>4</sup> Symptoms such as palpitations and persistent vomiting such as exhibited by our patient are known to have occurred.<sup>4</sup> Time taken to deplete the body's store of thiamine is thought to be approximately 3 weeks.<sup>5</sup>

Wernicke's encephalopathy is a well known sequelae of thiamine deficiency, most commonly seen in patients with chronic alcohol abuse. Prevalence in non-alcoholic patients varies from 0.04% to 0.13%, the most frequent settings being malignant disease (18.1%), post gastrointestinal surgery (16.8%), and hyperemesis gravidarum (12.2%).<sup>6,7</sup> It is characterised by the classic triad of encephalopathy, ophthalmoplegia and ataxia. Our patient had exhibited two of these. If left untreated, Wernicke's encephalopathy in the pregnant patient could progress to permanent neurological deficits, cognitive impairment and Korsakoff syndrome which can be fatal in up to 10-20% of cases; whereas in the foetus only about half of affected pregnancies will result in the birth of a normal baby, as it may lead to miscarriage, preterm birth, and also intrauterine growth retardation.<sup>6,7</sup>

Carbohydrate loading in a patient with thiamine deficiency may precipitate Wernicke's encephalopathy, hence it is highly recommended that in patients with suspected thiamine depletion, levels should first be taken and parenteral replacement instituted prior to commencing normal feeding or intravenous glucose.<sup>2</sup> There may also be a genetic predisposition as there is evidence of an abnormal form of transketolase that binds thiamine less avidly in patients who develop WE compared to that of controls.<sup>8</sup>

Our patient showed further neurological findings which were not consistent with Wernicke's encephalopathy, including reduced deep tendon reflexes, paraesthesia of extremities and progressive weakness of limbs. These peripheral neurological manifestations are all features of dry (neuritic) beriberi.<sup>4</sup> In dry beriberi there is usually symmetric, non-specific polyneuropathy with myelin degeneration and disruption of motor, sensory and reflex arcs.<sup>3</sup> It has a tendency to affect the legs before extending to the arms with sensory loss being accompanied by muscular weakness and hypo- or areflexia.<sup>3</sup>

It is likely that our patient had a combination of factors that had led to her thiamine depleted state. Pregnancy is a high consumptive state which has been known to lead to thiamine deficiency.<sup>4</sup> Pernicious vomiting in her 1st trimester also has led her into a thiamine deficient state. Even though she received parenteral hydration, inadequate thiamine replacement may have resulted in her unable to replenish her thiamine stores. It is possible that this deficiency had further continued further into her 2nd trimester contributing to her persistent state of vomiting.

A variability of clinical features may be present in patients with thiamine deficiency. The delayed development and complexity of her neurological signs is a common pitfall in getting a timely clinical diagnosis, and late thiamine replacement may have even contributed to her miscarriage.<sup>6</sup>

## CONCLUSION

Thiamine deficiency manifesting with features suggestive of an overlap between Wernicke's encephalopathy and dry beriberi is rare. A high index of suspicion needs to be retained when pregnant patients present with prolonged vomiting and poor oral intake coupled with both central and peripheral neurological symptomatology. By missing such symptomatology further complications from beri-beri

and Wernicke's encephalopathy can occur and if unheeded can ultimately lead to fetal and even maternal death.

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