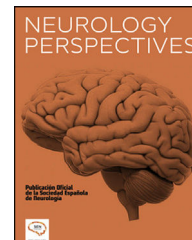




NEUROLOGY PERSPECTIVES

www.journals.elsevier.com/neurology-perspectives



SCIENTIFIC LETTER

Polyneuropathy in a pregnant woman with hyperemesis gravidarum: Do not forget dry beriberi



Polineuropatía en una gestante con hiperemesis gravídica: no olvides el beriberi seco

R. Ghosh^{a,1}, M. León-Ruiz^{b,1}, A.S. Mondal^c, S. Dubey^d, J. Benito-León^{e,f,g,h,*}

^a Department of General Medicine, Burdwan Medical College and Hospital, Burdwan, West Bengal, India

^b Section of Clinical Neurophysiology, Department of Neurology, University Hospital "La Paz", Madrid, Spain

^c Department of Neuromedicine, Bankura Sammilani Medical College and Hospital, Bankura, West Bengal, India

^d Department of Neuromedicine, Bangur Institute of Neurosciences, Kolkata, West Bengal, India

^e Department of Neurology, University Hospital "12 de Octubre", Madrid, Spain

^f Research Institute (i+12), University Hospital "12 de Octubre", Madrid, Spain

^g Centro de Investigación Biomédica en Red Sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain

^h Department of Medicine, Complutense University, Madrid, Spain

Received 25 July 2023; accepted 18 August 2023

Available online 1 October 2023

Dear Editor,

Beriberi, a treatable thiamine (vitamin B1) deficiency disease, may present as dry beriberi (commonly as symmetric sensorimotor polyneuropathy) and wet beriberi (with heart failure, with or without polyneuropathy).¹

Thiamine deficiency can result from reduced thiamine intake due to alcohol abuse, anorexia nervosa, dieting, or malabsorption following bariatric surgery.^{2,3} Malabsorption may also occur in patients with diarrhea, celiac disease, tropical sprue, or dysentery.⁴ Other less common causes of thiamine deficiency are burns, pregnancy, dialysis, and malignancy.² Dry beriberi has been exceptionally reported after hyperemesis gravidarum.⁵

We report the case of dry beriberi associated with polyneuropathy without Wernicke's encephalopathy due to severe thiamine deficiency following inadequately managed hyperemesis gravidarum.

A 20-year-old female from an extremely low socio-economic background from rural West Bengal, India, visited the outpatient clinic for severe disabling weakness involving all 4 limbs for the last 2 months.

She had a confirmed twin pregnancy following 6 months of marriage at the age of 19 years. She had severe hyperemesis gravidarum during pregnancy and could not eat due to persistent nausea and vomiting. As the pregnancy reached the term, she was complaining about tingling and numbness in a length-dependent stockings and gloves pattern, gait unsteadiness, slippage of chappals while walking, and extremely irritable mood. She got to the hospital for delivery and could walk with some support. She had twins delivered by cesarean section who were healthy. During the post-operative recovery period, she complained of difficulty walking, mild weakness in the distal upper limbs, and a remarkable worsening of paresthesias. She was discharged after 5 days without a formal neurological workup. At 2 months post-partum, she was completely bedridden and could not even care for the infants, and this time, she visited us.

A general examination revealed tell-tale signs of chronic malnutrition, i.e., low body mass index, mouth ulcers,

* Corresponding author.

E-mail address: jbenitol67@gmail.com (J. Benito-León).

¹ RG and ML-R had equal contributions and can be considered joint first authors.

angular cheilitis and atrophic glossitis, anemia, lustreless skin, conjunctiva, and hair. Hemodynamic parameters were however uncompromised.

On neurological examination, she had a low mood, bilateral lower motor neuron-type facial weakness (right more than left), quadripareisis (lower limbs more affected than upper limbs; distal more than proximal), small muscle wasting of distal lower and upper limbs, and absent deep tendon reflexes. Sensory examination revealed a length-dependent stockings and gloves pattern decreased pain and temperature sensation and reduced joint position and vibration senses (below knee level in inferior limbs and the wrist level in superior extremities), and pseudoathetosis. A gait examination revealed sensory ataxia. Autonomic and cerebellar functions were unremarkable.

Blood tests revealed microcytic hypochromic anemia (hemoglobin 8.9 g/dL) with raised erythrocyte sedimentation rate (60 mm/h) because of iron deficiency, mild hypocalcemia (corrected calcium 7.6 mg/dL), hyponatremia (130 meq/L), hypochloremia (93 meq/L), and hypokalemia (3.2 meq/L), low creatinine (0.5 mg/dL) levels (normal urinalysis), hypoalbuminemia (serum albumin 2.9 mg/dL), and mild transaminitis (AST 78 IU/L, ALT 82 IU/L). Serum CPK was normal. Serum vitamin B12, B6, and folate levels were normal, except for vitamin B1 (8 µg/L; n. 28–85; by high-performance liquid chromatography), and vitamin D (14.8 ng/mL) levels were extremely low. The thyroid panel revealed non-thyroidal illness syndrome. A nerve conduction study revealed axonal-type sensory-motor polyneuropathy, and electromyography showed chronic neuropathic features (reinnervation) with signs of activity (denervation). Magnetic resonance imaging of the brain and spinal cord was unremarkable. Serological tests for HIV (1, 2), HBV, HCV, and syphilis were negative. Skin biopsy for leprosy was negative. Anti-ganglioside antibodies profile was negative. Electrocardiogram, echocardiography, and NT pro-BNP levels were normal.

A diagnosis of dry beriberi with polyneuropathy was made, with psychiatric symptoms because of multi-factorial thiamine deficiency: (1) poor dietary habits due to low socio-economic status, (2) pregnancy itself (due to supply-demand mismatch) and associated hyperemesis gravidarum (aggravated by primigravid status, and multi-fetal gestation), and (3) lactation (again due to supply-demand mismatch and no therapeutic replenishment).

She was prescribed thiamine (1500 mg/day) intravenously (IV) for 5 days, followed by 500 mg/day for another 2 weeks, alongside a parenteral ferric carboxymaltose infusion of 1000 mg (as a single dose). And then, she was discharged home with oral benfotiamine 150 mg/day and strict dietary rehabilitation advice, including niacin supplementation. At 3 months follow-up after discharge, she entered the clinic unsupported. Sensory symptoms and motor weakness improved significantly but with mild small muscle wasting and absent deep tendon reflexes.

As far as we know, there is only 1 reported case of beriberi due to thiamine deficiency in a hyperemesis gravidarum patient, but unlike our case, was a long-lasting hyperemesis gravidarum associated with Wernicke's encephalopathy and wet beriberi.⁵

Thiamine deficiency can result in beriberi, either "dry" (without fluid retention) or "wet" (associated with cardiac failure with edema).^{1,6} Beriberi is characterized primarily by neuromuscular symptoms and usually occurs in populations relying exclusively on polished rice for food and older people or low-income groups with poor diets.^{1,6}

Thiamine is a water-soluble vitamin that plays a key role in cell metabolism, specifically in the Krebs cycle.^{1,7} The human body has a limited storage capacity for thiamine, with an average amount of 25–30 mg stored at any time.¹ The minimum daily requirement of thiamine is 0.3 mg/1000 kcal dietary intake in normal subjects, but the requirement is higher during pregnancy and old age. A 50–100 mg/day target is often used for therapeutic purposes.⁸

Thiamine depletion can occur quickly (within approximately 14 days of reduced thiamine intake).¹ Early symptoms are appetite loss, constipation, and nausea. They may progress to depression, peripheral polyneuropathy, and unsteadiness.^{1,6} Further deterioration results in mental confusion (loss of short-term memory), ataxia, and eye discoordination (Wernicke-Korsakoff's syndrome).^{1,6}

Dry beriberi is characterized by polyneuropathy, which has a severity that correlates with the degree and duration of thiamine deficiency.^{9,10} Affected patients complain of paresthesias or foot pain, with difficulty walking.^{9,10} The most common neurological finding is distal sensory loss, and weakness appears first in the finger and wrist extensors and the ankle dorsiflexion, and ankle stretch reflexes are lost in most patients.^{9,10} Polyneuropathy generally develops over weeks or months. Also, severe thiamine deficiency may lead to axonal abnormalities and impaired acetylcholine transmission.^{9,10} These axonal injuries may result in ataxia, areflexia, and painful sensory or sensorimotor polyneuropathy, accompanied by severe muscle weakness.^{9,10} Electrodiagnostic studies show axonal polyneuropathy with reduced amplitude of sensory or motor responses, normal or mildly reduced conduction velocity, and neuropathic changes.^{9,10} Unlike our case, it can be associated with Wernicke's encephalopathy and Korsakoff's syndrome.¹

Diagnosis of thiamine deficiency is based on the clinical features in the context of nutritional deficiency or high metabolic demands.⁸ Thiamine levels in serum and urine may be decreased, although the levels do not truly reflect tissue concentrations.⁸ Erythrocyte transketolase activity level depends on thiamine and provides an assay of functional status.⁸ The pyruvate accumulates during thiamine deficiency, and elevated serum level provides a supplementary diagnosis. A blood sample extraction should be performed before initiation of treatment because these laboratory abnormalities rapidly normalize.⁸

Treatment of thiamine deficiency consists of parenteral administration of 100 mg/d, which may be given IV in the acute stage.⁸ In the case of Wernicke's encephalopathy, thiamine is administered in a dose of 500 mg intravenously thrice daily for 2 days (in slow administration) and then 500 mg once daily for at least 5 days.¹¹ Long-term treatment includes a balanced diet, oral thiamine supplements, and other vitamins. The gradual return of sensory and motor

function can be expected after thiamine replenishment. In severe cases, improvement may last many months and be incomplete.¹⁰ It is recommended to associate other B vitamins orally (especially niacin) since adequate treatment only with thiamine alone can aggravate the neurological clinical state or trigger associated pellagra, especially in alcoholic patients.^{11,12}

Our case highlights the importance of not waiting for a person at risk of thiamine deficiency until the onset of polyneuropathy symptoms to replenish thiamine. Physicians must be able to recognize beriberi symptoms in hyperemesis gravidarum cases, as early replenishment can prevent polyneuropathy, Wernicke-Korsakoff' syndrome, and heart failure, especially in regions where complementary tests are not readily available, like developing countries.

Disclosures

Dr. Ritwik Ghosh (ritwikmed2014@gmail.com) reports no relevant disclosures.

Dr. Moisés León-Ruiz (pistolpete271285@hotmail.com) reports no relevant disclosures.

Dr. Abdus Samim Mondal (samimmondal1621@yahoo.com) reports no relevant disclosures.

Dr. Souvik Dubey (drsouvik79@gmail.com) reports no relevant disclosures.

Dr. Julián Benito-León (jbenitol67@gmail.com) reports no relevant disclosures.

Study funding

This study has not been funded.

Patient consent

Written informed consent was obtained from the patient participating in the study.

Ethical considerations

Written informed consent was obtained from the patient participating in the study.

Author contributions

All authors contributed significantly to the creation of this manuscript; each fulfilled criterion as established by the ICMJE.

Conflicts of interests

The authors do not have any conflict of interest.

Acknowledgments

J. Benito-León is supported by the National Institutes of Health, Bethesda, MD, USA (NINDS #R01 NS39422), the European Commission (grant ICT-2011- 287739, NeuroTREMOR), the Ministry of Economy and Competitiveness (grant RTC-2015-3967-1, NetMD—platform for the tracking of movement disorder), and the Spanish Health Research Agency (grant FIS PI12/01602 and grant FIS PI16/00451).

References

- Shible AA, Ramadurai D, Gergen D, Reynolds PM. Dry beriberi due to thiamine deficiency associated with peripheral neuropathy and Wernicke's encephalopathy mimicking Guillain-Barré syndrome: a case report and review of the literature. *Am J Case Rep.* 2019;20:330–4. <https://doi.org/10.12659/AJCR.914051> PMID: 30862772.
- Sriram K, Manzanares W, Joseph K. Thiamine in nutrition therapy. *Nutr Clin Pract.* 2012;27:41–50. <https://doi.org/10.1177/0884533611426149> PMID: 22223666.
- Wilson RB. Pathophysiology, prevention, and treatment of beriberi after gastric surgery. *Nutr Rev.* 2020;78:1015–29. <https://doi.org/10.1093/nutrit/nuaa004> PMID: 32388553.
- World Health Organization, Office of the United Nations High Commissioner for Refugees. *Thiamine Deficiency and Its Prevention and Control in Major Emergencies.* Geneva: World Health Organization; 1999 (Micronutrient series).
- Indraccolo U, Gentile G, Pomili G, Luzzi G, Villani C. Thiamine deficiency and beriberi features in a patient with hyperemesis gravidarum. *Nutrition.* 2005;21:967–8. <https://doi.org/10.1016/j.nut.2005.04.001> PMID: 15979284.
- Dominiczak MH. Vitamins and minerals. Water-soluble vitamins. B-complex vitamins. In: Baynes JW, Dominiczak MH, editors. *Medical Biochemistry.* 5th ed. Philadelphia: Elsevier; 2019. p. 78–83.
- Bâ A. Metabolic and structural role of thiamine in nervous tissues. *Cell Mol Neurobiol.* 2008;28:923–31. <https://doi.org/10.1007/s10571-008-9297-7> PMID: 18642074.
- J. Jankovic, J.C. Mazziotta, S.L. Pomeroy and N.J. Newman, Deficiency diseases of the nervous system. *Thiamine deficiency neuropathy (Beriberi)*, In: *Bradley and Daroff's Neurology in Clinical Practice*, 8th edition, 2022, Elsevier Inc; Philadelphia, 1296.
- J. Hamel, E. L. Logigian. Acute nutritional axonal neuropathy. *Muscle Nerve.* 2018; 57: 33-39. <https://doi.org/10.1002/mus.25702>. PMID: 28556429.
- R. Nardone, Y. Höller, M. Storti, M. Christova, F. Tezzon, S. Golaszewski, et al. Thiamine deficiency induced neurochemical, neuroanatomical, and neuropsychological alterations: a reappraisal. *ScientificWorldJournal.* 2013;2013:309143. <https://doi.org/10.1155/2013/309143>. PMID: 24235882.
- Martínez Salio A, Romero Muñoz JP. *Enfermedades carenciales.* In: Camacho Salas A, González de la Aleja Tejera J, Sepúlveda Sánchez JM, editors. *Urgencias en neurología.* 2nd ed. Madrid: Hospital universitario 12 de Octubre, Ergon; 2012. p. 416–9.
- Redzic S, Hashmi MF, Gupta V. Niacin deficiency. [Updated 2023 Feb 19]. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557728/>.