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CASE REPORT

Thiamine Deficiency in the Pathophysiology and Diagnosis of Wernicke-Korsakoff Syndrome: Case Report and Literature Review

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Abstract

Thiamine deficiency is associated with life-threatening pathologies, as Wernicke syndrome (WS), Korsakoff syndrome (KS), Marchiafava-Bignami (MB) disease, and wet or dry beri-beri (BB). Among the etiological factors, the thiamine deficiency may be suspected in subjects at risk for malnutrition (decreased nutrient intake, increased nutrient losses, or impaired nutrient absorption). Computed tomography (CT) but especially magnetic resonance imaging (MRI) is the best method to detect diencephalic and mesencephalic cytotoxic edematous lesions in patients with acute WS, with hyperintense on long-TR spin-echo MRI imaging and low-density signal abnormalities on CT scans. We report a case of WS in an 82-year-old woman with the history of cancer and eating disorder, who presented a neurological worsening during recovery, associated with low serum thiamine levels and the presence of symmetrical areas of hyperintense signal in the long-TR sequences of MRI. After parenteral thiamine supplementation, we observed a rapid improvement of ocular and language disorders occurred, with a low and incomplete improvement of peripheral neuropathy, supporting the WS diagnosis. Our case report presented the clinical picture of WS and KS and the diagnosis was confirmed by both the laboratory tests and the brain imaging techniques. The dosage of the vitamin was useful and accurate when performed before the beginning of the supplementation therapy. This case is important in bringing to light a clinical picture often observed in many medical recovery units.

Keywords Thiamine deficiency · Wernicke syndrome · Korsakoff syndrome · Magnetic resonance imaging · Case report

Introduction

Thiamine deficiency is associated with life-threatening pathologies, as Wernicke syndrome (WS), Korsakoff syndrome (KS), Marchiafava-Bignami (MB) disease, and wet or dry beri-beri (BB) (beriberi literally means "I can't, I can't" in Singhalese) [1].

Among the etiological factors, the thiamine deficiency may be suspected in subjects at risk for malnutrition (decreased nutrient intake, increased nutrient losses, or impaired nutrient absorption) by chronic alcohol abuse, long-term fasting, hunger strike, gastric surgery, bariatric surgery, malabsorption, hyperemesis gravidarum, cancer, HIV infection, chronic renal failure, severe sepsis, burns or chronic long-term parenteral nutrition [2–5].

Among brain imaging techniques CT but especially MRI is the best method to detect diencephalic and mesencephalic cytotoxic edematous lesions in patients with acute WS, with hyperintense on long-TR spin-echo MRI imaging and low-density signal abnormalities on CT scans [6, 7]. The thiamin deficiency usually involves bilateral, symmetric and selective brain structures, as the diencephalic paraventricular region of thalamus (anterior and medial nuclei) (CT/MRI), the mesencephalic periaqueductal gray matter (MRI), the mamillary bodies (MRI), the tectal plate (the inferior and superior colliculi) (MRI). Atypical lesions are in the cerebellum, vermis, cranial nerve nuclei, red nuclei, dentate nuclei, caudate nuclei, splenium and cerebral cortex [8].

The sensitivity of CT and MRI is low: 13% and 53%, respectively, with a high number of false negative cases [6]. On the contrary the specificity is high (93% for MRI), with

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a low number of false positive cases [6]. Therefore, normal findings on brain imaging technique do not exclude the diagnosis of acute WS, that should be based on clinical and laboratory features.

When the thiamine deficiency becomes chronic (as in the patients KS), the brain correlated abnormalities are the mamillary body, cerebellar and cerebral shrinkage [9].

The thiamine deficiency may be identified by the laboratory tests, i.e. the indirect erythrocyte transketolase activity assay and the accurate direct measurement of thiamine by high-performance liquid chromatography (HPLC) [8].

We report a case of WS in a woman with the history of cancer and eating disorder.

Case Report

A 82-year-old woman was admitted to hospital with a 7-day history of lack of appetite, vomiting, dysphagia, fatigue, with a syncopal episode the day before the admission. She had a past medical history of a left urothelial renal carcinoma treated by nephrectomy (pTa, N0) in 2013, a bladder recurrence treated by total cystectomy and bilateral hysteroannessiectomy with a right ureterocutaneostomy in 2014 (with ureteral catheter positioning), a subsequent urethrectomy of the external urethral meatus for a local recurrence in 2020. Moreover, she presented with recurrent urinary tract infections, a recent clostridium colitis, a stage 3 chronic kidney disease, anemia, chronic inflammatory condition, alloimmunization by repeated blood transfusions, pulmonary nodules, nodular goiter, previous cholecystectomy in 2018, diffuse osteoarthritis (hips and knees), chronic eating disorder, and decreased mobility syndrome.

The culture tests, at different times during her stay, revealed the presence of *Enterococcus faecalis* (urine), *Enterococcus faecium* and *Escherichia coli MDR* (urine), *Clostridium difficile* (fecal sample), *Staphylococcus haemolyticus* (blood), *Staphylococcus capitis* (blood), *Staphylococcus pettenkoferi* (blood), *Candida parapsilosis* (blood), and the patient received specific antibiotic therapies with fosfomycin, tigecycline, ceftazidim/avibactam, daptomycin, fidaxomicin, and capsofungin, respectively. The right mono J 8 Ch ureteral catheter was changed every 28 days.

Cerebral, abdominal, and thoracic computed tomography scan showed a brain atrophy, a multinodular thyroid, bilateral lung micronodules, surgical urinary outcomes, right ureteral catheter, cortical cysts and post-logistic scarring of the right kidney.

Due to the worsening of her clinical status, the appearance of dysphagia and the concomitant systemic infection, the patient was not able to maintain an adequate nutrition. For this reason, intravenous fluid therapy was administered with normal saline solution and glucose 5% solution and parenteral nutrition was started (960–1440 ml/day), continued for approximately 30 days.

One month after the admission, the patient presented a neurological worsening, with comprehension and motor disorder of language, convergent strabismus, anisocoric eyes (left > right), horizontal nystagmus, diffuse hyposthenia more evident to the left arm. At this point, a brain CT scan was performed, in order to proceed with diagnostic investigation: it showed a mild fronto-parietal periventricular leukoencephalopathy and atrophic dilation of the supratentorial ventricular system and subarachnoid spaces, without acute injures.

According to the malnutrition status of the patient, due to severe and prolonged diarrhea related to relapsing Clostridium colitis and the protract parental nutrition in absence of other supplement intake, we suspected a vitamin deficiency encephalopathy.

The dosage of serum thiamine levels has been requested as soon as the suspicion was raised and just before starting supplementation therapy.

The MRI revealed the presence of symmetrical areas of hyperintense signal in the long-TR sequences, bilaterally localized in the hypothalamic, ventro-medial thalamic, quadrigeminal lamina and periaqueductal space region; the supratentorial ventricular system was enlarged and the mild dilation of the liquor spaces was confirmed (Fig. 1A–C).

Therefore, parental thiamine supplementation was started, administering 100 mg/day intramuscularly added with a polyvitamic supplement intravenously (thiamine 2.5 mg, riboflavin 3.6 mg, nicotinamide, biotin, cyanocobalamin, and others) for 40 days.

Due to strong clinical suspicion, parenteral thiamine supplementation was started before getting the serum thiamine levels results, which later turned out to be equal to 9.6 mcg/l (normal value 28–85 by HPLC), confirming the diagnosis.

Parental nutrition was replaced by enteral administration through a nasogastric tube.

A rapid improvement of ocular and language disorders occurred, with a low and incomplete improvement of peripheral neuropathy.

When the clinical conditions allowed it, nasogastric tube was removed and we started oral feeding, prescribing semi-soli board and high-protein and high-calorie nutritional supplement (200 mL tid) until the end of the recovery. We prescribed thiamine oral administration (300 mg/day) after stopping the parental supplementation.

Discussion and Conclusions

The WS syndrome classically is an acute triad of oculomotor abnormalities, gait ataxia, and a confusional state, described by Carl Wernicke in 1881 [10]. The KS syndrome

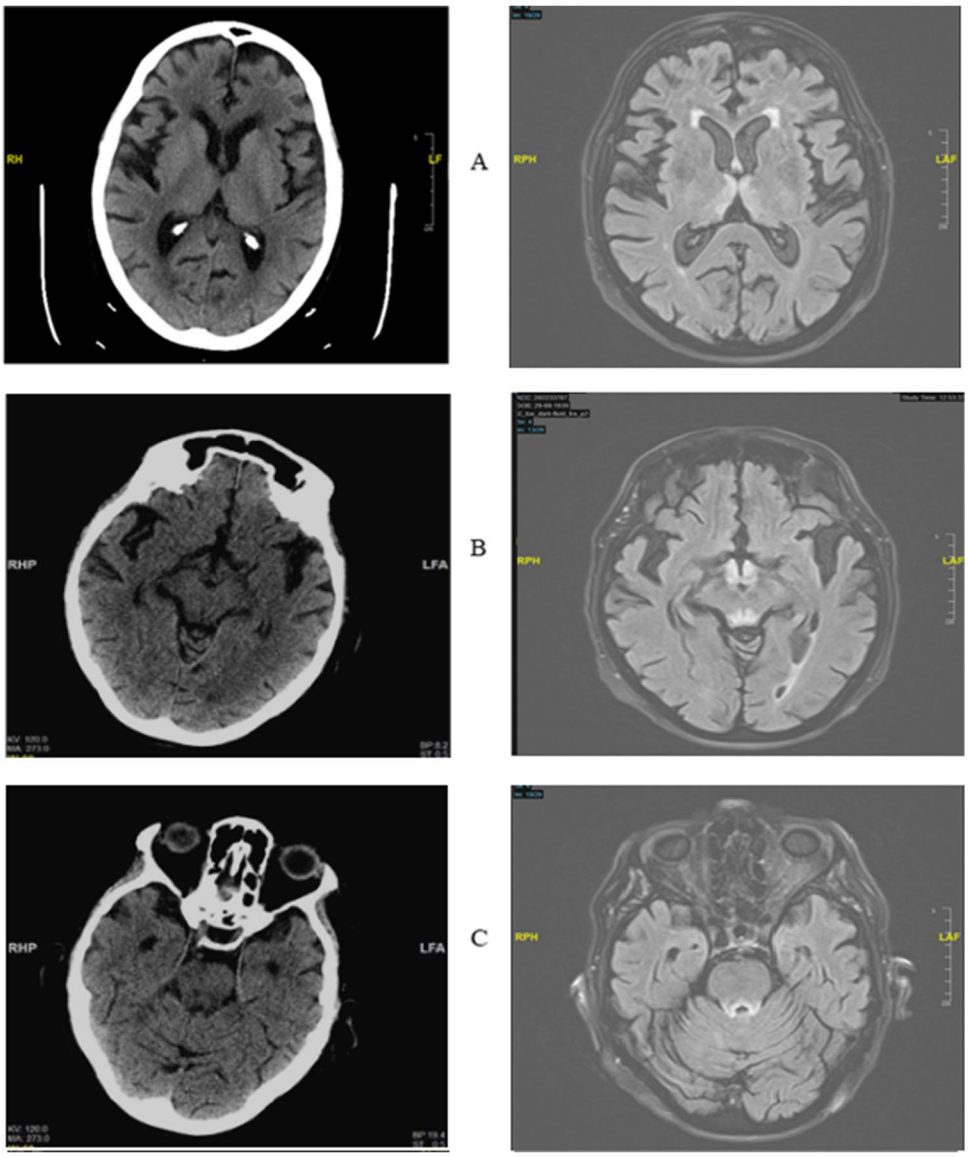

Fig. 1 CT scans and MR imaging at the level of the bilateral thalamus (**A**), mammillary bodies and tectal plate (**B**), and the periaqueductal gray matter (**C**), showing MRI T2/FLAIR symmetrically increased signal intensity

is a chronic alteration characterized by severe memory loss with anterograde amnesia, confabulation, disorientation, with psychosis and hallucinations, firstly reported in 1887 in ''About alcoholic paralysis'' by Sergey Sergeevich Korsakoff for his medical doctorate thesis [11]. The MB disease is linked to the demyelination/necrosis of the corpus callosum and the near subcortical white matter with a wide array of symptoms including altered mental state, loss of consciousness and epileptic seizures, impaired walking, dysarthria, pyramidal signs with spasticity, and dementia, discovered in 1903 by Ettore Marchiafava and Amico Bignami [12]. The wet BB is characterized in infants by cardiovascular involvement with lactic acidosis, vasodilation, tachycardia, high output heart failure, pulmonary, and peripheral edema [13, 14]. The dry BB is identified in adolescents by a peripheral sensorimotor polyneuropathy with parasthesias, muscle weakness and/or pain of the upper and lower extremities [2]. It has been reported that the disease called Jiao Qi (equivalent to modern BB) was prevalent in the medieval China [15]. The gastroenterologic symptoms of slow gastric emptying, nausea, vomiting, jejunal dilatation, megacolon, and constipation may accompany the cardiovascular and neurological alterations of thiamine deficiency [2]. The BB etiology remained unknown in Asia, where it was frequent due to the diet deficiency for the polished white rice, until the thiamine was isolated in 1911 by the Japanese Umetaro Suzuki and Torai Shinamura [16] and then synthetized in 1936 by Robert Williams and Joseph Cline at Merck laboratories of New York [17], starting to treat the disease by the supplementation [12].

Excluding the classical BB syndromes (not frequent in western countries) and the more evident KS and MB disease,

the complete clinical picture of WS is only present in one third of cases and the disease may be underdiagnosed [18]. It is well known that WS disorder is typically found in alcohol use disorder. The fact that it also occurs in nonalcoholic patients is otherwise often ignored [19], supporting how this case is important in bringing to light a clinical picture often observed in many medical recovery units.

The patient of the case report presented the clinical picture of WS and KS and the diagnosis was confirmed by both the laboratory tests and the brain imaging techniques.

The dosage of the vitamin was useful and accurate when performed before the beginning of the supplementation therapy, but to the extent that it does not delay the start of therapy.

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Data Availability Original data and material.

Code Availability Not applicable.

Declarations

Ethics Approval It is a case report, and ethics approval is not applicable.

Consent to Participate Written informed consent was obtained from the patient.

Consent to Publication Written permission has been obtained from the participant for publication.

Conflicts of Interests The authors declare that they have no conflict of interest.

References

1. Smith TJ, Johnson CR, Koshy R, Hess SY, Qureshi UA, Mynak ML, et al. Thiamine deficiency disorders: a clinical perspective. Ann N Y Acad Sci. 2021;1498:9–28.
2. Frank LL. Thiamin in clinical practice. J Parenter Enteral Nutr. 2015;39:503–20.
3. Manzanares W, Hardy G. Thiamine supplementation in the critically ill. Curr Opin Clin Nutr Metab Care. 2011;14:610–7.
4. Unsal MA, Kaya D. An underestimated diagnosis in practice: Wernicke encephalopathy in two patients with cancer. J Neurol Sci. 2017;34:194–8.
5. Basoglu M, Yetimalar Y, Gurgor N, Buyukcatalbaş S, Kurt T, Secil Y, et al. Neurological complications of prolonged hunger strike. Eur J Neurol. 2006;13:1089–97.
6. Antunez E, Estruch R, Cardenal C, Nicolas JM, Fernandez-SoIa J, Urbano-Marquez A. Usefulness of CT and MR imaging in the diagnosis of acute Wernicke's encephalopathy. Am J Radiol. 1998;171:1131–7.
7. Zuccoli G, Pipitone N. Neuroimaging findings in acute Wernicke's encephalopathy: review of the literature. AJR Am J Roentgenol. 2009;192:501–8.
8. Galvin R, Brathen G, Ivashynka A, Hillbomd M, Tanasescu R, Leone MA. EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol. 2010;17:1408–18.
9. Bigler DE, Nelson JE, Schmidt RD. Mamillary body atrophy identified by magnetic resonance imaging in alcohol amnestic (Korsakoff) syndrome. Neuropsychiatry Neuropsychol Behav Neurol. 1989;2:189–201.
10. Wernicke C. Die acute, hämorrhagische Polioencephalitis superior. In: Lehrbuch der gehirnkrankheiten für aerzte und studierende. Kassel & Berlin. Ed. von Theodor Fischer 1881, vol.II, 229–242.
11. Korsakoff SS. Eine psychische störung combinirt mit multipler neuritis. Allgem Zschr Psychiatr. 1890;47:475–85.
12. Marchiafava E, Bignami A. Sopra un'alterazione del corpo calloso osservata in soggetti alcoolisti. Riv Patol Nerv Ment. 1903;8:544–9.
13. Gubbay ER. Beri-Beri heart disease. Can Med Assoc J. 1966;95:21–7.
14. Wenckebach KF. St. Cyres lecture on heart and circulation in a tropical avitaminosis (beri-beri). Lancet 1928;2:265.
15. Fan KW. Jiao Qi disease in medieval China. Am J Chin Med. 2004;32:999–1011.
16. Suzuki U, Shimamura T. Value of polished rice as a food stuff, and the beriberi disease of animal. Tokyo Kagaku Kaishi. 1911;32:4–17 (in Japanese).
17. Williams RR, Cline JK. Synthesis of vitamin B1. J Am Chem Soc. 1936;58:1504–5.
18. Mateos-Díaz AM, Marcos M, Chamorro AJ. Síndrome de Wernicke-Korsakoff y otras patologías asociadas al déficit de tiamina. Med Clin (Barc). 2022;9:431–6.
19. Oudman E, Wijnia JW, Oey MJ, van Dam M, Postma A. Wernicke-Korsakoff syndrome despite no alcohol abuse: a summary of systematic reports. J Neurol Sci. 2021;426(February):117482.