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Prolonged emesis as prodromal symptom and exacerbating factor of non-alcoholic Wernicke-Korsakoff Syndrome: a costly diagnostic delay

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ABSTRACT

Background. Wernicke–Korsakoff syndrome (WKS) is a serious neurological disorder caused by thiamine (vitamin B1) deficiency. The term refers to two different conditions. Wernicke encephalopathy (WE) is an acute syndrome related to the deficiency. It requires early diagnosis and emergent treatment to prevent long term consequences and even death. Korsakoff syndrome (KS) refers to the progression into chronic and irreversible amnestic-confabulatory syndrome. While WKS is better known to affect people with alcohol use disorder, it can be also associated with other causes of malnourishment, like bariatric surgery or hyperemesis gravidarum. WE is clinically late-diagnosed because of lower prevalence in non-alcoholic population. On some occasions, prolonged vomiting can be a cause, a prodromal symptom before neurological manifestations and an exacerbating factor.
Case presentation. We present a case of a 72-year-old woman with a history of gastrointestinal resection. The patient was admitted to our hospital because of recurrent emesis and worsening of neurological signs. She was previously admitted to another hospital, where doctors excessively focused on gastrointestinal symptoms, thus causing an important diagnostic delay.
Conclusions. Prevention has a prominent role in WKS. Ensuring an adequate diet, identifying risk factors and subsequently recognizing and promptly treating with intravenous vitamin supplementation are crucial to prevent devastating consequences.

INTRODUCTION

Wernicke–Korsakoff syndrome (WKS) is the most common encephalopathy caused by the deficiency of a single vitamin, vitamin B1 or thiamine [1]. It is a devastating neurological disorder that requires emergency treatment to prevent permanent damage or even death. Thiamine deficiency causes neurological and behavioral impairment, and it is classified into two different conditions. Wernicke encephalopathy (WE) is caused by acute deficiency of vitamin B1. It is characterized by a distinctive triad involving ocular disturbances (ophthalmoplegia), cerebellar dysfunction (ataxia) and changes in mental state (confusion). If not properly treated, signs and symptoms of WE can progress into Korsakoff syndrome (KS), which is an irreversible amnestic-confabulatory syndrome. WE is often lately diagnosed due to lower prevalence in the non-alcoholic population and complex clinical presentation. It mainly affects people with alcohol use disorder (AUD), and it is responsible for up to 59%

of all deaths from alcohol abuse [2]. Several studies demonstrated that WE is associated with other causes of malnourishment [3], *e.g.*, malabsorption, low dietary intake, nervous anorexia, hyperemesis gravidarum (HG) and recurrent vomiting, parenteral nutrition not accompanied by proper supplementation [4], sepsis, gastrointestinal diseases and gastrointestinal surgery, especially bariatric procedures [5]. On some occasions, prolonged emesis can be a cause, a prodromal symptom before neurological manifestations and an exacerbating factor. Preventing malnutrition, and promptly diagnosing and treating thiamine deficiency are crucial to avoid progression towards an irretrievable neurological damage.
Here we present a case of WKS occurred in a 72-year-old woman.

CASE PRESENTATION

A 72-year-old woman was admitted to our hospital because of recurrent vomiting and worsening of neurological signs. She had a history of hypertension, previous poliomyelitis, biliopancreatic diversion (BPD) surgery as treatment for pathological obesity performed 14 years earlier, foregoing intestinal sub-occlusion occurred 7 years earlier, and antecedent vertebral surgery for spinal cord cancer not-otherwise-specified. She was independent in activities of daily living (ADL) and instrumental activities of daily living (IADL) previously to the acute event.
She was just discharged against medical advice from another hospital by the will of her relatives because of worsening of her clinical conditions. Previous treating physicians suspected psychogenic emesis, for which they started treatment with benzodiazepines. Family reported that she had started suffering from nausea and recurrent emesis after receiving the booster shot of Pfizer vaccine. For this reason, after 15 days she was conducted to the previous hospital.
According to the medical records of the previous admission, the patient was prescribed fasting and parenteral electrolyte solutions for 15 days. After that, she gradually resumed oral feeding (mainly hot tea and rusks) for 4 more days, until discharge. Note that, even before admission, the patient suffered from conditions that compromised an adequate nutritional intake, *i.e.*, persistent emesis. After that, she was carrying on with a very poor oral nutrition and parenteral electrolyte solutions as support, without any other nutritional supplementation. Moreover, the patient's mental state was worsening, progressing towards a permanently disoriented status.
On admission she presented confused, arousable to intense verbal stimuli, asthenic, not oriented, unable to reply to simple questions nor to execute simple orders. Her abdomen was slightly distended and diffusely tender with no peritoneal signs. On neurological examination, she presented marked weakness of the lower limbs and mild weakness in the upper limbs with positive Mingazzini test bilaterally, without sensitivity deficit. She also showed corrective saccadic movements during the pursuit test and bilateral dysmetria of the finger-nose-finger test, signs of cerebellar dysfunction. Physical examination of heart, lungs and skin was normal.
The brain CT did not show intracranial haemorrhages nor recent ischemic events.
Blood tests showed mild leucocytosis and mild hyponatremia, which was corrected via intravenous therapy. Ammonia and markers of renal and hepatic function were within normal ranges. Also, TSH, T4, folates and vitamin B12 were within reference values. Vitamin D and A were low. On the sidelines, she tested positive at molecular SARS-CoV-2 nasopharyngeal swab, which was performed as requested by internal protocols.
Abdominal CT showed moderate wall thickening, supported by oedema of the tenual submucosal between the gastrointestinal anastomosis and the tenuous-tenual anastomosis. These findings were compatible with inflammatory-infectious alterations.
EEG documented modest diffuse slowing, without any asymmetries, focal abnormalities, or epileptic alterations.
During hospitalization, the patient presented with marked thrombocytopenia, which contraindicated the execution of cerebrospinal fluid (CSF) tests. As an alternative, serology for neurotropic viruses (Cytomegalovirus, Epstein Barr Virus, and Parvovirus B19) was required, which resulted negative.
Brain MRI was scheduled, but it was prematurely interrupted due to the patient's agitation. In this occasion, only non-diagnostic T2w and DWI sagittal images were acquired.
The measurement of thiamine levels in the blood was not carried out due to a lack of reagents in the laboratory of our hospital. In consideration of the

previous bariatric surgery, of the patient's recent clinical history suggestive of a prolonged state of malnutrition and malabsorption, in consideration of the neuroradiological and neurophysiological findings, empiric therapy with intravenous thiamine (100 mg every 8 hours) was prescribed, in association with multivitamin complexes.
After two weeks, a new brain MRI was performed (**Figure 1**). It showed T2-FLAIR alteration in the periaqueductal area (midbrain tegmentum), the mesial nuclei of the thalamus and the anterior columns of the fornix. These findings were compatible with Wernicke-Korsakoff encephalopathy [6].
The patient's cognitive status progressively improved. However, she presented residual paraplegia with failure to recover the standing position and significant alteration of memory.

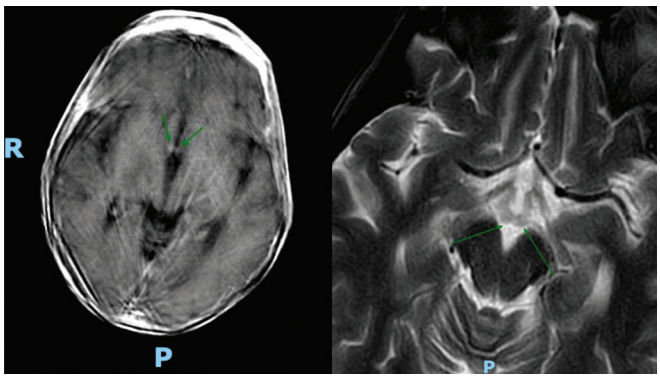

Figure 1. *MRI. T2/FLAIR images showed alteration of midbrain tegmentum (posterior periacqueductal region, right), and mesial thalamic nuclei and anterior columns of the fornix (left), compatible with the diagnosis Wernicke Encephalopaty.*
R: right; P: caudal.

DISCUSSION

Clinical presentation, MRI findings, and the improving of the symptoms after vitamin supplementation support the diagnosis of thiamine deficiency. Thiamine dosage was not possible in our laboratory, so other diagnostic hypotheses were ruled out through neurophysiological and laboratory exams, and imaging.
Prolonged reduction in nutritional intake, accompanied by malabsorption and emesis, caused multivitamin deficiency in a patient with a pre-existent risk factor (gastrointestinal resection). Unfortunately, the admission to the previous hospital and a wrong diagnosis of psychogenic emesis caused an important diagnostic delay and the persistence of residual disability.
Patients who undergo bariatric surgery are lifetime susceptible to malabsorption and vitamin deficiency [7]. Their risk of vitamin deficiency is higher in presence of concurrent factors like infections, pregnancy, malnourishment, or alcohol abuse. Therefore, prevention has a prominent role for WKS.
In gynecologic patients, HG is a possible cause of non-alcoholic WKS. It usually occurs in the first trimester. In HG, like in patients who underwent bariatric procedures, nausea, vomiting, blurring of vision or diplopia occur before the onset of neurological symptoms. Nutritional demands, including thiamine, are increased in pregnancy [8, 9]. In the first trimester, recurrent emesis and inadequate food intake can exasperate nutritional deficiencies [10, 11].

CONCLUSIONS

Probably, identifying risk factors for the development of WE, ensuring an adequate diet, and subsequently recognizing and promptly treating with intravenous vitamin supplementation, could have prevented permanent residual disability. Both physician and surgeons should identify patients with high risk of developing vitamin deficiencies, such as alcohol abusers, subjects undergoing rapid weight loss, with prolonged malabsorption and episodes of emesis. In this specific case, during the previous hospitalization, the doctors focused on gastrointestinal symptoms, overlooking the importance of providing the patient with sufficient nutritional intake. At discharge, the patient was prescribed vitamin oral supplementation. However, there will never be a total remission of the neurological symptoms.

COMPLIANCE WITH ETHICAL STANDARDS

Authors contribution

E.L., F.F., E.M.: Conceptualization. E.L., F.F., M.A., F.M., E.M.: Investigation. F.F., M.A., F.M., E.M., R.B., F.L.: Project administration. E.L., F.F., S.C., E.M., R.B., F.L.: Methodology. E.L., F.F., S.C.: Visualization. E.L.: Writing – original draft. E.L., F.F., S.C., M.A., F.M., E.M., R.B., F.L.: Writing – review & editing. E.M., R.B., F.L.: Supervision. E.M., R.B., F.L.: Validation. All authors read and approved the final version.

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Study registration

N/A.

Disclosure of interests

The authors declare that they have no conflict of interests.

Ethical approval

N/A.

Informed consent

Written informed consent was obtained from the patient for publication of this research.

Data sharing

Data are available under reasonable request to the corresponding author. The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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