

## Wernicke's Encephalopathy: An Overlooked Cause

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### Abstract

A 66-year-old female patient with a past medical history of obesity and ORBERA<sup>®</sup> intragastric balloon placement presented with Wernicke's encephalopathy (WE) features without social history of alcoholism. The patient was subjected to ORBERA<sup>®</sup> balloon bariatric procedure in Egypt and subsequently developed episodes of uncontrolled emesis which prompted removal of the intragastric balloon placement one month later. Two weeks after removal of the intragastric balloon placement, vomiting still persisted. Patient suddenly developed altered mental status and weakness which prompted admission to our hospital. Initial clinical examination was largely inconclusive, bilateral horizontal nystagmus was noted after subsequent days. A tentative diagnosis of WE was made based on clinical presentation and magnetic resonance imaging (MRI) scan results; vitamin B1 (thiamine) levels were ordered but were still pending. Empiric treatment with vitamin B1 infusion was initiated which resulted in improvement of both motor function and cognitive functions. Patient was given 200 mg IV TID for 8 days, then 100 mg po for 6 months. Patient was also started on folic acid and vitamin B12. WE diagnosis was supported one week later after lab results showed low vitamin B1 level (21 nmol/L). The patient was sent to rehabilitation center for 6 weeks then was able to be discharged home with a 6-month supply of vitamin B1 supplements. On discharge, memory deficits, loss of appetite and docility were noted.

### Keywords

Intragastric balloon placement, Vitamin B1, Non-alcoholic Wernicke's encephalopathy, Balloon placement reversal, Obesity, Thiamine, Gastric, Clinical nutrition, MRI, T2 FLAIR sequences, ORBERA<sup>®</sup>

### Introduction

Wernicke's encephalopathy (WE) is a neurological emergency caused by vitamin B1 deficiency. Chronic alcoholism is the most commonly known cause [1, 2]. In non-alcoholic population, history of total parenteral nutrition, eating disorders, multiple bowel surgeries, chemotherapy and conditions such as hyperemesis gravidarum are risk factors for WE [1, 3-11]. Despite several reports, diagnosis of WE is commonly delayed or overlooked [3]. Roux-en-Y gastric bypass has been frequently associated with nutritional deficiencies by causing early satiety and malabsorption. Complications are seen less often in restrictive procedures such as intragastric balloon placement [4, 5]. Of the few reported Wernicke's syndrome involving ORBERA<sup>®</sup> placement cases one out of the three reported cases were fatal. The fatal case was undiagnosed until autopsy

report came back [6] which revealed mammillary body necrosis. Prognosis of WE depends on prompt diagnosis and management [7]. The estimated mortality rate of WE is close to 20 percent [8].

## Case Presentation

A 66-year-old female with a past medical history of obesity, recent ORBERA® intragastric balloon placement in Egypt and status post gastric balloon reversal in USA one-month prior, presented to the ER for intractable vomiting that has been continuous for one month. Since reversal of gastric balloon placement patient presented with recent onset of altered mental status and generalized weakness. A gastric balloon reversal was done a four weeks after its placement in an attempt to alleviate patient's emesis; however, patient's symptoms persisted four weeks after the removal of the device. Patient's BMI decreased from 35 kg/m<sup>2</sup> to 26 kg/m<sup>2</sup> following the procedure. Family member reported that they previously visited two additional hospitals prior visiting our ER complaining of the same symptoms but her deteriorating mental status and weakness were overlooked. Patient has no significant past history of organic psychiatric disorders or alcohol/drug use.

During the early hospital course, the patient was noted to be minimally verbal, inattentive with depressed affect and difficult to comprehend due to abnormal speech pattern. Patient refused meals stating not being hungry and grimaced on abdominal palpation. The patient later became somnolent and unable to stay awake or follow verbal commands. When awake, patient complained of headache, feeling "sad", severe weakness and fatigue. Urinary incontinence was then reported. On day two, the patient was uncooperative, showing evidence of bilateral horizontal nystagmus, left abducens palsy and unable to perform finger-nose-finger test. Temporal disorientation, further confusion and mild agitation were later witnessed.

No evidence of psychiatry disorder was noted. To rule out other causes, TSH, vitamin B12, folate, LFTs, RPR, ammonia, serum copper, zinc, calcium and phosphate were analyzed and all were within normal limits. At this time, vitamin B1 levels were still pending. Magnesium was slightly elevated (2.6 mg/dL). Lumbar puncture was performed to rule out viral/bacterial meningitis and CSF analysis was unremarkable.

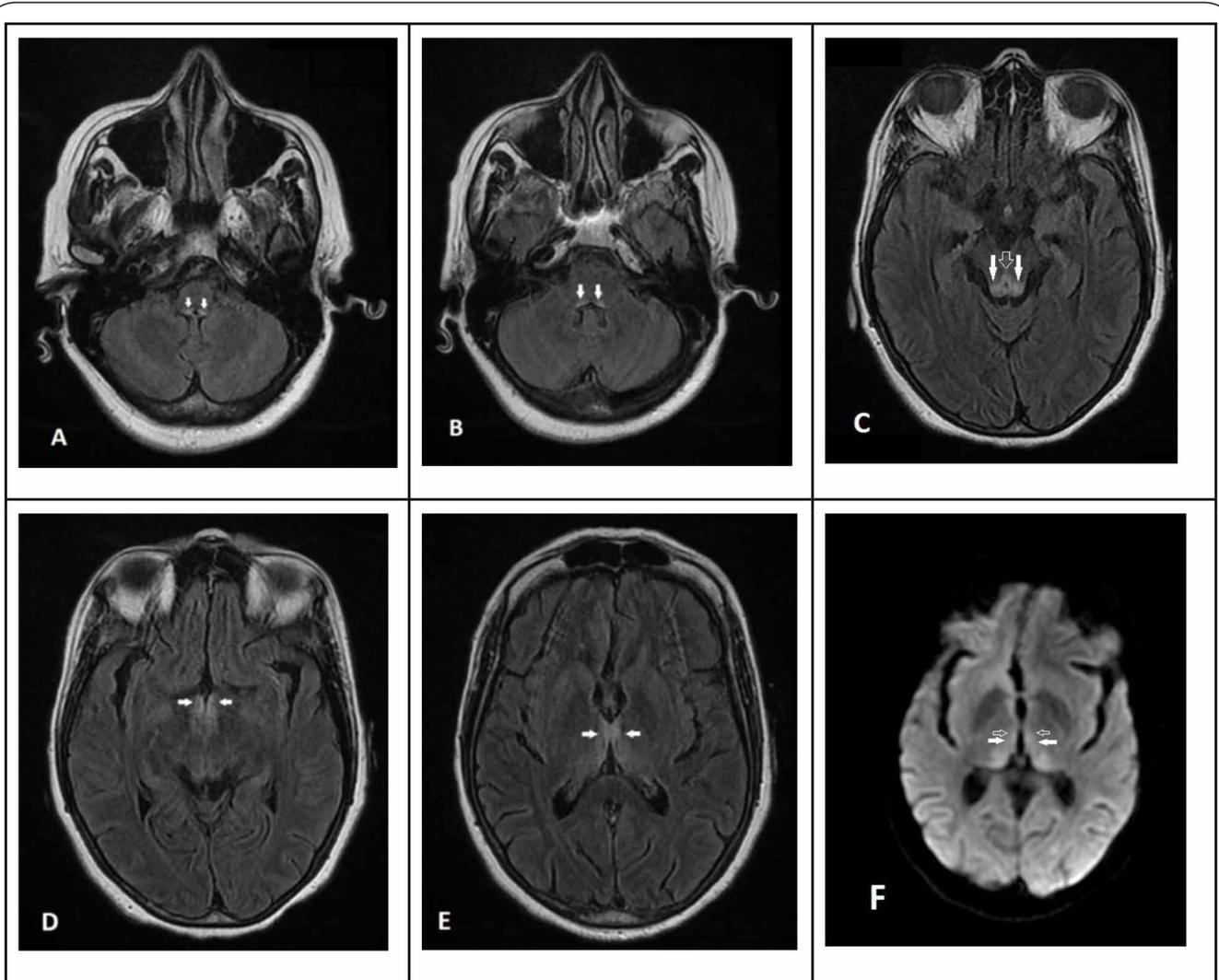
MRI revealed a high signal abnormality within the periaqueductal gray matter of the midbrain and the periventricular gray matter bordering the third ventricle. It also revealed hyper intense signals on T2 and FLAIR sequences involving mammillary bodies along with contrast enhancement and diffusion restriction. These MRI findings can be appreciated in [figure 1](#). On the basis of clinical presentation and MRI findings, diagnosis of WE was confirmed. Patient was started on vitamin B1 and gradually recovered; however, mild amnesia was still noted days after. Vitamin B1 results were obtained eventually: 21 nmol/L (reference range 78-185 nmol/L) which also further supported our diagnosis. We considered testing pyruvate and transketolase levels; however, results would not modify management of care.

## Discussion

The recent increase in the use of bariatric surgery and procedures worldwide has been associated with an increased incidence of WE [9, 10]. Of 104 reported cases of WE after bariatric surgery, 84 cases were gastric bypass [9]. Micronutrient deficiencies following gastric bypass were evaluated in 957 patients. A total of 236 (25%) had vitamin B12 deficiency and 11 (1%) had vitamin B1 deficiency. Frequent vomiting was a risk factor for these deficiencies in about 90% of the cases [9]. Continuous vomiting depletes vitamin B1 levels in 3 - 6 weeks. Vitamin B1 deficiency presents with neurologic impairments as in Wernicke's encephalopathy and polyneuropathy [11, 12]. Altered levels of Magnesium can be seen in WE since the active form of thiamine: thiamine pyrophosphate, requires Magnesium as a cofactor [8].

The triad of WE (ophthalmoplegia, ataxia and confusion) is not always present which can interfere with clinicians from accurately making the diagnosis. Triad occurs only in about 30% of cases [3]. Early symptoms mostly presents as frequent headaches, fatigue, irritability and abdominal discomfort. These symptoms progress to spatial/temporal disorientation, apathy, agitation and hallucination [8]. Impaired cognition in patients with WE may preclude an accurate initial diagnosis. Fortunately, neuroimaging has improved diagnostic accuracy and also allows differentiation of acute versus chronic stages of WE. MRI specificity is 93% on patients affected with this condition [13]. Acutely, these lesions can be visualized as increased intensity signal on magnetic resonance imaging which reflects an edematous state in the brain. Affected regions of the brain include the periventricular nuclei, medial vestibular nuclei, abducens nuclei, periaqueductal gray matter, mammillary bodies, hypothalamic nuclei, tectal plate and thalamus. Chronic states reveal mammillary bodies' atrophy, cortical thinning, sulcal widening and ventriculomegaly [2].

Impaired anterograde amnesia, fatigability, awareness and consciousness, as seen in this case, has been associated with lesions to the mammillary bodies [8, 14] and, the latter, periaqueductal gray matter [15]; these anatomical site were hyperintense on MRI. Other symptoms such as conjugate horizontal gaze on physical examination can be explained by hyperintensity located at abducens nuclei [16]. Periventricular nuclei injuries, again noted on MRI, have been associated with urine incontinence since it is part of the supraspinal brain circuitry regulating micturition [17]. Medial vestibular nuclei injury has been linked to symptoms like ataxia of gait and stance, dizziness and vertigo [18]. Cranial nerve palsy occurs due to an injury on cranial nerve VI nuclei. Patients are unable to produce a conjugate horizontal gaze on physical examination. Fortunately, abducens function improves shortly after parenteral administration of Thiamine [16]. Mammillary bodies along with the dorsomedial and anterior nuclei of the thalamus play an active role in memory formation. More specifically, lesions in the mammillary bodies have been implicated with anterograde amnesia, fatigability and unawareness [14]. MRI findings along with clinical signs and symptoms provide reliable approach to diagnose WE [15].



**Figure 1:** 66 y/o non-alcoholic female with history of intragastric balloon placement and reversal. MRI was performed on a 1.5 Tesla magnet. T2 FLAIR sequences revealed hyperintensity in the (A) medial vestibular nuclei, (B) abducens nuclei, (C) tectum of the midbrain (solid arrows) and periaqueductal grey matter (transparent arrow), (D) mammillary bodies, (E) medial thalami and periventricular region of the third ventricle. Diffusion weighted imaging (F) also revealed multiple regions of restricted diffusion including the medial thalamus (solid arrows) and periventricular region of the third ventricle (transparent arrows). Findings are consistent with diagnosis of Wernicke's encephalopathy.

The WE treatment was often insufficient, specifically ignoring low parenteral thiamine levels (77.2%). In case of suspicion, thiamine levels should be tested and treated adequately with parenteral thiamine supplementation [10]. Current guidelines for bariatric surgery suggest preventive thiamine supplementation (12 mg) in multivitamin treatment for all patients undergoing surgery, but higher doses for patients with suspicion for deficiency [7]. All bariatric procedures can lead to deficiencies and therefore to WE. WE can be fully prevented by supplying prophylactic thiamine given either parenterally in vomiting patients or orally in non-vomiting patients [10]. WE onsets suggests that bariatric patients remain more vulnerable to vitamin B1 deficiency for life, and therefore require lifelong routine follow-up on their B1 status [10].

## Conclusion

The incidence of WE after restrictive bypass procedure has increased; yet, many physicians are not aware of it. Our

patient visited two separate hospitals for persistent vomiting before being admitted at our facility, however WE suspicion was overlooked. From this case we emphasize the importance of having a high suspicion index for vitamin deficiencies in patients with any history of intragastric balloon/ bariatric procedure and prolonged unretractable emesis. We also want to highlight that WE can still develop even if intragastric balloon placement is reversed. In the absence of the classic triad, MRI imaging can play a crucial role in the diagnosis of WE. The prognosis of WE depends on prompt diagnosis and vitamin B1 supplementation. In our case patient was given 200 mg IV TID for 8 days, then 100 mg PO for 6 months. Patient was also started on folic acid and vitamin B12. In the absence of early diagnosis and management, WE can evolve into Korsakoff syndrome or death.

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## Conflict of Interest

The authors have no conflict of interest to be disclosed.

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