

## Case Report

# Wernicke's encephalopathy in a patient with unresectable gastric carcinoma and literature review

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Received October 20, 2014; Accepted January 7, 2015; Epub January 15, 2015; Published January 30, 2015

**Abstract:** Wernicke's encephalopathy (WE) is a disease classically associated with nutrition deficiency. It is characterized by typical symptoms like confusion, ataxia and ophthalmoparesis, and develops due to thiamine deficiency in alcoholic patients. Recently, it has been shown that WE could occur in patients with gastric carcinoma without a history of alcohol use. In this paper, we have made some suggestions about early diagnosis, treatment and prevention of WE by discussing the development of WE in a patient with unresectable gastric carcinoma, who had been inpatient for a long time and given radiotherapy and chemotherapy.

**Keywords:** Wernicke's encephalopathy, chemoradiotherapy, parenteral nutrition

## Introduction

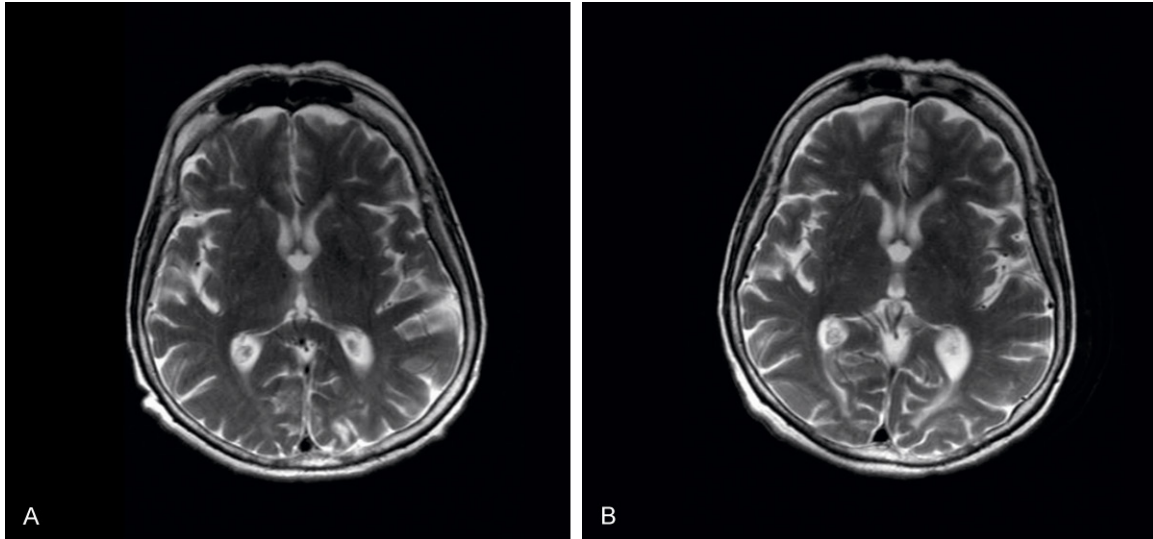
Wernicke's encephalopathy (WE), which arises from thiamine deficiency, is a neuropsychiatric syndrome causing significant morbidity and mortality. It is characterized by symptoms like confusion, ataxia, and ophthalmoparesis [1]. Thiamine deficiency occurs during chronic malnutrition (long-term alcohol use, cancer, hunger strike, hyperemesis gravidarum), and acutely after gastrointestinal bariatric surgery [2, 3]. The development of WE after parenteral nutrition without thiamine supplementation was first reported in 1975 by Blennow [4]. Only about 20% of the cases can be defined from the relevant literature, with the rest unnoticed and thus unreported [5].

Even though WE is common in patients with alcohol addiction, it is important to be aware that it can also occur in non-alcoholic patients. Health care providers, including nutritionists, should be aware of the symptoms and findings of this disease and recognize those at risk for early intervention. This case is presented to emphasize that the duration of radiotherapy is important and risky for the development of WE

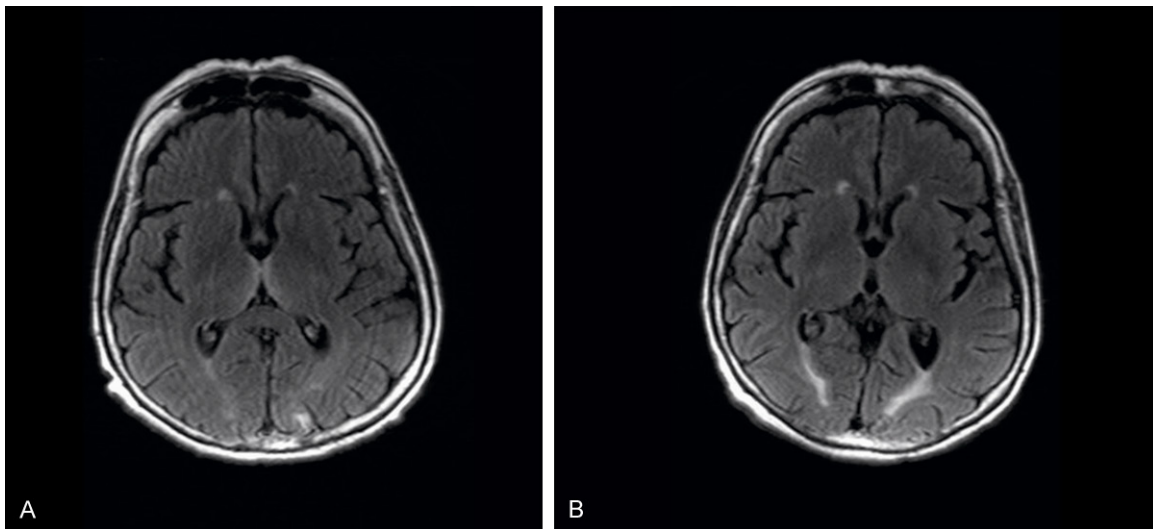
in long-term hospitalized patients with gastric carcinoma receiving parenteral nutrition (PN).

## Case report

A sixty four-year old woman with no history of alcohol use and any other comorbidity was diagnosed with gastric carcinoma that was located in the lesser curvature and antrum endoscopically. Positron emission tomography and computed tomography scanning of the thorax and abdomen revealed no evidence of distant metastasis. Explorative surgery of the stomach revealed gastric carcinoma with indistinguishable demarcation of the liver. Regional lymph node metastasis was evident and the tumor was evaluated as unresectable. Subsequently, the patient was given neoadjuvant chemotherapy that consisted of cisplatin, 5-Fluorouracil and folinic acid. After neoadjuvant chemotherapy the patient was evaluated for surgery but the tumor was considered as unresectable. Subsequently, concurrent chemoradiotherapy was started because of gastric bleeding from the tumor. During the treatment, since the patient could not tolerate oral nutrition because of nausea and vomiting, parenteral nutrition was initiated.



**Figure 1.** Bilaterally symmetrical signal augmentation in the medial parts of thalamus next to the third ventricle on the T2A axial images (A). Loss of the signal after the treatment in the same localization on the T2A axial images (B).

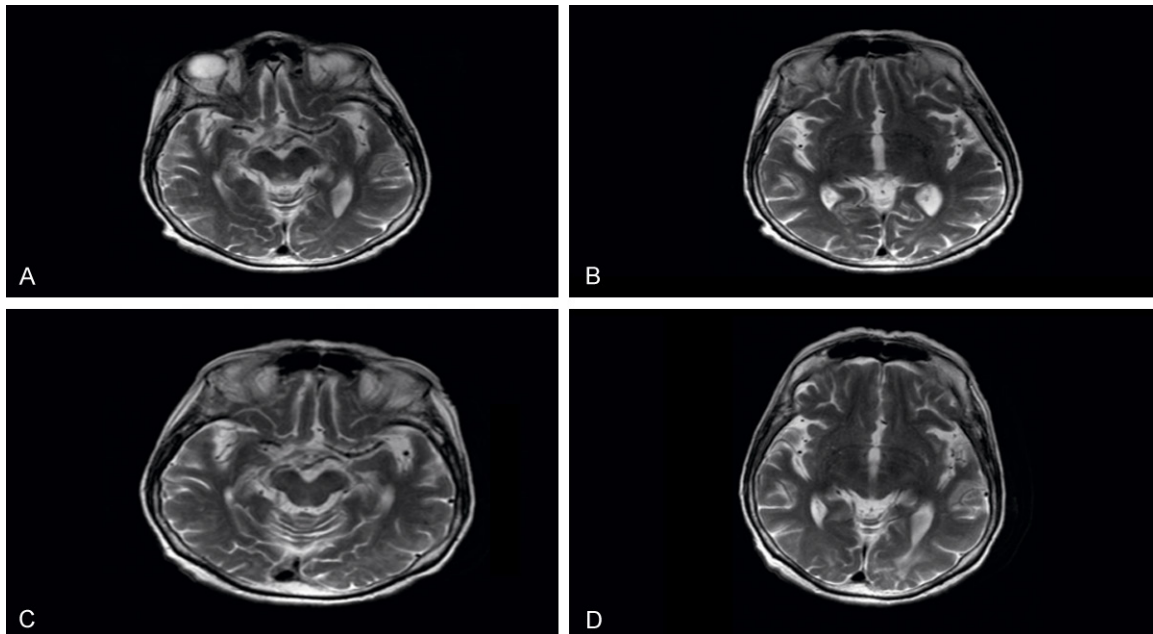


**Figure 2.** Bilaterally increased symmetrical signals in the medial parts of the thalamus next to the third ventricle on the FLAIR axial images (A). Normal signal in the same localization on the FLAIR axial images after treatment (B).

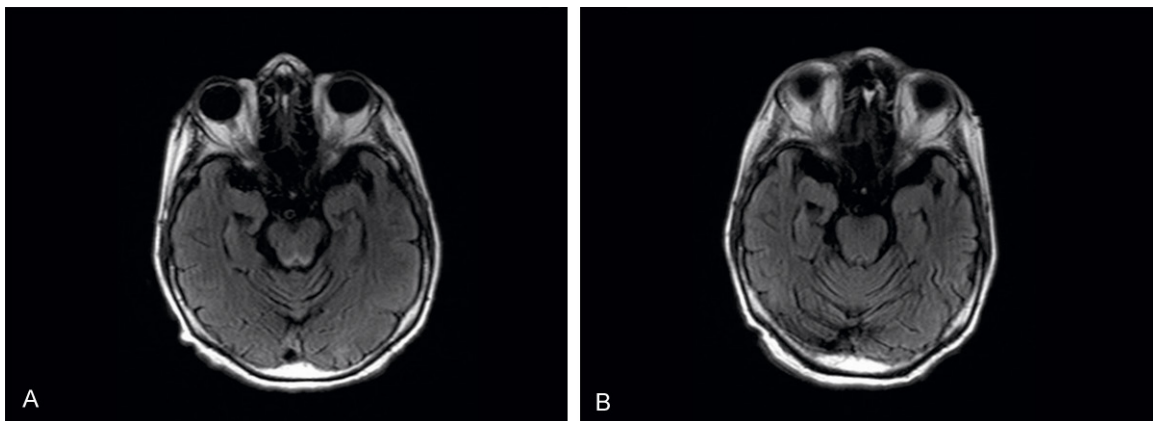
During the third week of radiotherapy, the patient presented with severe nausea and vomiting, confusion, diminishing vision, limitation of sight, and weakness in the lower extremities. At this stage, we suspected cranial metastasis and had cranial magnetic resonance imaging (MRI) with contrast taken. In the cranial MRI, there were bilaterally increased symmetrical signals in the medial parts of the thalamus next to the ventricle (**Figures 1A** and **2A**), abnormal hyperintense signals in the periaqueductal gray matter (**Figures 3A, 3B** and **4A**), and hyperin-

tense signals on the T2A axial and FLAIR images in the periaqueductal gray matter on DAG images (**Figure 5A**).

Based on the clinical presentation and the radiological findings, non-alcoholic WE diagnosis was made. Thiamine was administered for two days at 600 mg/day parenterally, followed by 200 mg/day for five days, 100 mg/day for one week, and a maintenance dose of 25 mg/day from then on. All symptoms regressed from the second day on and returned to normal in



**Figure 3.** Abnormal hyperintense T2A signal in the periaqueductal gray matter (A, B). Normal T2A signal in the same localization after treatment (C, D).



**Figure 4.** Abnormal hyperintense FLAIR signal in the periaqueductal gray matter (A). Normal FLAIR signal in same localization after treatment (B).

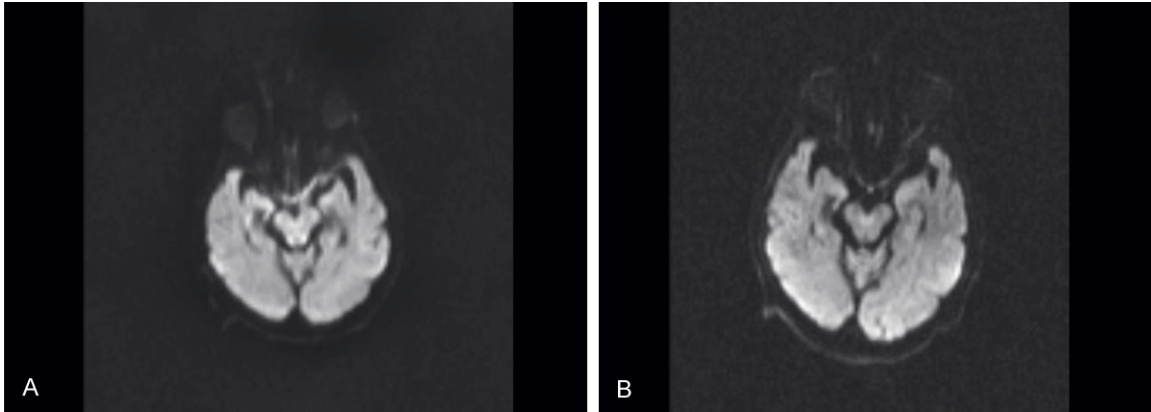
the second week. Cranial MRI images taken 3 weeks after the initiation of therapy with thiamine revealed no abnormalities (**Figures 1B, 2B, 3C, 3D, 4B and 5B**).

#### Discussion

Despite better survival rates in gastric carcinomas because of improved treatment techniques and better supportive care with parenteral nutrition, the risk of developing WE has increased owing to chemotherapy and radiotherapy causing nausea-vomiting, gastrointes-

tinal obstruction, and inadequate nutrition. Because of lack of awareness of these predisposing circumstances, it is very likely that WE is under reported [6, 7]. In our case, the patient not only remained hospitalised for five months but also underwent two explorative surgical interventions, received chemotherapy and radiotherapy and parenteral nutrition, which made her prone to developing WE.

In a study reporting similar cases, non-alcoholic WE developed in patients with gastric carcinoma, who had surgery and were on total par-



**Figure 5.** Abnormal hyperintense signal in the periaqueductal gray matter and medial thalami on diffusion-weighted images (A). Normal signal in the periaqueductal gray matter and medial thalami on diffusion-weighted images after treatment (B).

enteral nutrition. Improvement of symptoms in five of the seven patients was recorded after thiamine therapy [7]. In another report, autopsy findings of a WE case revealed that non-therapeutic intervention resulted in death, which might have been prevented by thiamine administration [8].

Total parenteral nutrition (TPN) increases thiamine consumption by the kreb cycle, thus creating a relative shortage of the vitamin. However, in poor oral nutrition cases (Table 1), insufficient or total absence of vitamin intake is in question.

The efficiency of thiamine absorption from the stomach is likely to be more pronounced in the distal part. This is supported by the literature where the location of the stomach lesion is stated (Table 1).

The most susceptible age group for WE is 28 to 71 and the most common symptom is ataxia, which was also the case in our patient (Table 1 and [2, 6-10]).

To facilitate the diagnosis of WE, the clinical features of the disease were classified in accordance with its stage as follows: symptoms at presentation, uncommon at presentation, and late-stage as shown in Table 2 [1].

Clinical settings related to Wernicke's encephalopathy include the following conditions: Staple diet of polished rice, surgical procedures (gastrectomy, gastrojejunostomy, partial or subtotal colectomy, gastric bypass surgery, vertical

banded gastroplasty, therapy with an intragastric balloon), gastrointestinal disorders (peptic ulcer, gastric cancer, colon cancer, ulcerative colitis with megacolon, recurrent vomiting or chronic diarrhoea, pyloric stenosis, drug-induced gastritis, biliary colics, Crohn's disease, intestinal obstruction or perforation, lithium-induced diarrhoe, migraine attacks, anorexia nervosa, pancreatitis, hyperemesis gravidarum), severe obesity, cancer and related conditions (gastric carcinoma non-Hodgkin's lymphoma, myelomonocytic leukaemia, large B-cell lymphoma, myeloid leukaemia, allogenic bone marrow transplantation), systemic conditions (renal diseases, AIDS, chronic infectious febrile diseases, thyrotoxicosis, magnesium depletion, chronic diuretic therapy), intravenous infusion of high-dose nitroglycerin or tolazamide, absolute food/thiamine deficiency (dietary restrictions owing to economic reasons or political trade embargoes, psychogenic food refusal, prolonged fasting for religious-philosophical reasons, starvation for treatment of obesity, hunger strike, neglect in old age or Alzheimer's disease), relative thiamine deficiency (unbalanced total parenteral nutrition, unbalanced intravenous hyperalimentation, re-feeding syndrome, use of dietary commercial formulae, slimming diets, excessive cooking of food, chronic use of food containing thiaminases or antithiamine factors, and chronic use of sulphites as food additives (in dogs).

Typical MRI findings of WE include symmetrically increased abnormal signal intensities on the T2-weighted and FLAIR images of the peri-

## Wernicke's encephalopathy post-gastric chemoradiotherapy

**Table 1.** Characteristics of Wernicke's encephalopathy in gastric cancer patients

Reference	Sex/Age	Localization	Operation	Nutrition Type	Symptoms	Thiamine provision	Type of imaging	Outcome
Kondo [2] 1996	F/28	Unknown	Inoperable	Total parenteral nutrition (TPN)	Ataxia, Confusion, Diplopia, Dizziness	Yes	Unknown	Improved
Weiauer [9] 2004	F/71	Unknown	Unknown	Unknown	Ataxia, Confusion, Nystagmus	Yes	MRI	Not Improved
Onishi [10] 2004	F/66	Unknown	Inoperable	TPN	Disorientation, Delusion, Insomnia	Yes	Unknown	Improved
Kim [11] 2006	M/65	Proximal Stomach	Total Gastrectomy	TPN	Ataxia, Disorientation, Dizziness	Yes	MRI	Unknown
Kim [11] 2006	F/71	Unknown	Subtotal Gastrectomy	TPN	Confusion, Disorientation, Nystagmus	Yes	MRI	Improved
Eun [7] 2010	F/48	Esophageal Junction	Inoperable	TPN	Ataxia, Diplopia, Nystagmus	Yes	MRI	Improved
Eun [7] 2010	F/58	Unknown	Subtotal Gastrectomy	Oral	Ataxia, Confusion, Disorientation, Gaze Palsy, Seizure	Yes	MRI	Not Improved
Zuccoli [12] 2011	F/65	Unknown	Total Gastrectomy	Poor Oral Nutrition	Ataxia, Nystagmus, Stupor	Yes	MRI	Improved
Atay [6] 2011	M/32	Unknown	Inoperabl	TPN	Confusion, Nystagmus, Paraparesis	Yes	MRI	Improved
Hata [8] 2014	M/62	Unknown	Unknown	Oral	Ataxia, Confusion, Diplopia	No	Autopsi	Exitus
Desai [13] 2014	M/69	Pylorus	Subtotal Gastrectomy	Unknown	Oftalmoparesis, Nystagmus, Ataxia	Yes	MRI	Improved
Kudru [14] 2014	Unknown	Pylorus, Antrum	Subtotal Gastrectomy	Unknown	Nystagmus, Oftalmoparesis	Yes	MRI	Improved
Present case 2014	F/64	Antrum	Inoperable	TPN	Oftalmoparesis, Confision, Paraparesis	Yes	MRI	Improved

**Table 2.** Clinical features of Wernicke's encephalopathy

Common at presentation	Uncommon at presentation	Late-stage symptoms
Ocular abnormalities	Stupor	Hyperthermia
Mental status changes	Hypotension and tachycardia	Increased muscular tone and spastic paresis
Ataxia	Hypothermia	Choreic dyskinesias
	Bilateral visual disturbances and papilloedema	Coma
	Epileptic seizures	
	Hearing loss	
	Hallucinations and behavioural disturbances	

aqueductal gray matter of the mamillary body, medial thalamus, hypothalamus and middle brain [16]. In diffusion-weighted images, there may be decreased apparent diffusion coefficient values in these locations together with unusual contrast enhancement [17]. Cranial MRI is necessary for diagnosis of this disease in patients whose neurological status worsen, as this disease has such a wide range of symptoms. In our patient, neurological deterioration developed following a week-long severe vomiting. Cranial MRI pointed to WE, for which the patient was put on thiamine with immediate amelioration of the symptoms.

Diagnosis of WE in non-alcoholic patients with gastric carcinoma in early stage is difficult [6]. The symptoms of early stage WE are non-specific and it is difficult to differentiate encephalopathy caused by nutritional deficiency from the possible conditions in patients with gastric carcinoma complicated with cranial metastasis, electrolyte imbalances, hypoxia, uremia, sepsis, liver insufficiency and hypoglycaemic encephalopathy [18].

Continuous infusion of 5-Fluorouracil and low dose cisplatin used commonly in gastric carcinoma in chemotherapy can also cause neurotoxic effects in addition to vomiting, diarrhea, stomatitis, alopecia and mucositis [19].

The most common factors causing non-alcoholic WE are reported to include various surgical procedures like gastrectomy, cholecystectomy, intragastric balloon surgery, gastrojejunostomy, and gastric bypass surgery [15]. In addition to these, hyperemesis gravidarum, anorexia nervosa and AIDS are reported as predisposing factors.

During PN, thiamine requirement is increased since it is a required basic co-factor in the krebs cycle for transformation of pyruvate to acetyl coenzym A [2, 15, 20]. For this reason, thia-

mine support during PN could prevent the risk of developing WE.

### Conclusion

Nutritional disorders are common in patients with cancer, and PN is frequently used intentionally for support. WE related to PN is a preventable condition that occurs frequently in these patients. Occurrence of non-alcoholic WE is very likely in long-term inpatients on PN presenting neurological symptoms. It should be born in mind that chemoradiotherapy also constitutes one of the risk factors of this condition, as in our case, which is the first to be reported.

### Disclosure of conflict of interest

None.

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