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**Case Report**

# An Underestimated Diagnosis in Practice: Wernicke Encephalopathy in Two Patients With Cancer

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## Abstract

Impairment of mental status is frequently seen in cancer patients. Common causes are infection, metabolic disturbance, organ failure, medication, delirium or metastatic disease. Wernicke encephalopathy (WE) is likely to be underestimated in clinical practice in nonalcoholic population including this special patient group. The purpose of this paper is to take attention to WE and cancer concomitance, and emphasize the role of magnetic resonance imaging (MRI) in the early diagnosis of this complicated disease. We report two cancer patients who were consulted to our neurology department because of altered mental status and other neurological disabilities. When the patients underwent brain MRI for differential diagnosis, symmetrical perimidline lesions of the brain made the suspicion of WE diagnosis. In addition, one of the patient's MRI showed symmetric cortical and cerebellar involvement that is more typical in nonalcoholic form of WE. Both patients mostly recovered clinically, also showed concordant resolution of MRI abnormalities within 4-8 weeks after thiamine supplementation. WE diagnose should be kept in mind in cancer patients with altered mental status and thiamine treatment should be started during undergoing evaluation and differential diagnose to prevent irreversible clinical sequelae. Improved recognition of radiologists and well-known imaging findings of WE can facilitate early detection and effective treatment in nonalcoholic WE patients.

**Keywords:** Wernicke encephalopathy, thiamine deficiency, Wernicke encephalopathy in malignancy

# Pratikte Gözardı Edilen Bir Tanı: Kanser Hastalarında Wernicke Ensefalopatisi

## Özet

Kanser hastalarında şuurda bozulma oldukça sık görülür. Bu durumun en sık sebepleri enfeksiyonlar, metabolik bozukluklar, organ hasarları, ilaçlar, deliryum ve santral sinir sistemine metastazlardır. Wernicke Ensefalopatisi (WE) tanısı bu özel hasta grubunda alkolik olmayan diğer vakalarda olduğu hemen akla gelmez. Bu yazının amacı WE ve kanser birlikteliğine dikkati çekmek ve Manyetik Rezonans Görüntülemenin (MRG) bu kompleks hastalıktaki önemini vurgulamaktır. Biz şuurda bozulma nedeniyle kliniğimize danışılmış 2 hastayı sunduk. Hastalara ayırıcı tanılara yaklaşım açısından beyin MRG yapıldığında, simetrik orta hat lezyonları WE tanısını şüphelendirdi. Hastalardan birinin MRG'sinde alkolik olmayan WE vakalarında görülen şekilde kortikal ve serebellar lezyonlar da mevcuttu. Tiamin tedavisi sonrasında 4-8 hafta içerisinde, her iki hasta klinik ve radyolojik olarak düzelme gösterdi. Şuur bulanıklığı ile başvuran kanser hastalarında WE tanısı akılda tutulmalıdır.

Geriye dönüşsüz sekelleri önlemek amacıyla tiamin tedavisi ivedilikle başlanmalıdır. İyi tanınan radyolojik görünümler alkolik olmayan hastalarda da erken tanı ve efektif tedavinin önünü açacaktır.

**Anahtar Kelimeler:** Wernicke ensefalopatisi, tiamin eksikliği, kanser hastalarında Wernicke ensefalopatisi

## INTRODUCTION

Wernicke encephalopathy (WE) is a serious neurologic syndrome secondary to thiamine deficiency, which is clinically characterized by mental status changes, ocular abnormalities, and ataxia (1). Apart from chronic alcoholism, WE can be found in many different clinical settings such as cancer, chemotherapy, acquired immunodeficiency syndrome, prolonged therapeutic fasting, prolonged parenteral nutrition, bariatric surgery, prolonged vomiting, anorexia nervosa, systemic infectious and noninfectious diseases, and dietary imbalance (2). Prevalence studies of WE among nonalcoholics have not been performed, but cancer (18.1%) is the most common cause of non-alcoholic WE, followed by gastrointestinal surgery (16.8%) in the European Federation of the Neurological Societies (EFNS) guidelines (3).

Due to its low prevalence and nonspecific clinical presentation, patients with nonalcoholic WE are prone to misdiagnosis or diagnostic delay in clinical practice. High clinical suspicion and awareness of various typical and atypical magnetic resonance imaging (MRI) findings are essential for early diagnosis. MR imaging of the brain showing T2 and fluid-attenuated inversion recovery (FLAIR) hyperintensities in typical (thalami, mammillary bodies, tectal plate, and periaqueductal area) and atypical areas (cerebellum, cranial nerve nuclei, and cerebral cortex) is surely the most important and effective tool in the diagnostic assessment of WE. However, it should be kept in mind that only 31% of patients with cancer show typical MRI features of WE (4) .

A diagnosis of WE should be taken into consideration in patients with cancer because of its high morbidity and mortality.

Herein, we report two patients with cancer who were diagnosed as having WE.

## CASE PRESENTATION

### CASE 1

A woman aged 37 years with chronic myeloid leukemia was referred to our neurology department because of altered mental status. She had a prolonged hospital stay after an allogeneic bone marrow transplantation due to respiratory infection and malnutrition. She was receiving total parenteral nutrition (TPN) without multivitamin preparation. She was not oriented to place and time. A neurologic examination revealed loss of equilibrium with incoordination of gait and trunk ataxia. With the exception of multidirectional nystagmus, her ocular movements showed no abnormalities. Her cranial MRI revealed the following in T2-weighted imaging (T2WI) and FLAIR: Bilaterally symmetric hyperintensities in the medial thalami, periaqueductal area, bulbus and mammillary bodies (Figure 1A). Contrast enhancement was seen in the midbrain. Although examining serum thiamine levels was not available in our hospital, nystagmus, ataxia, and confusion with inadequate intake of thiamine due to the TPN, and her MRI images made us suspect WE. She was treated with 50 mg of intravenous thiamine twice daily. After she tolerated oral feeding, treatment was shifted to oral thiamine. One month later, her follow-up MRI showed resolution of abnormal signals and contrast enhancement (Figure 1B). After two months, her mental status

and neurologic status had recovered completely.

## CASE 2

A woman aged 67 years was admitted to the emergency department with diplopia, dysarthria, and severe ataxia. She had pancreatic cancer and reported loss of appetite and nausea, and diarrhea for a month. Her neurologic examination showed horizontal and vertical gaze-evoked nystagmus of both eyes, vertical gaze palsy, dysmetria, and severe ataxia. The cerebral MRI scan showed symmetric hyper-intense signals on T2WI and FLAIR in the bilateral ventromedial thalamus, frontobasal region of third ventricle, midbrain, cerebellar vermis, and bilateral cortical watershed zones (Figure 2A). The level of serum thiamine could not be measured, but her history of diarrhea and malignancy and MRI findings caused us to be suspicious of WE. Her symptoms vanished after two weeks of daily 100-mg thiamine therapy. One month later, a follow-up cranial MRI showed almost complete resolution of the abnormal signals (Figure 2B).

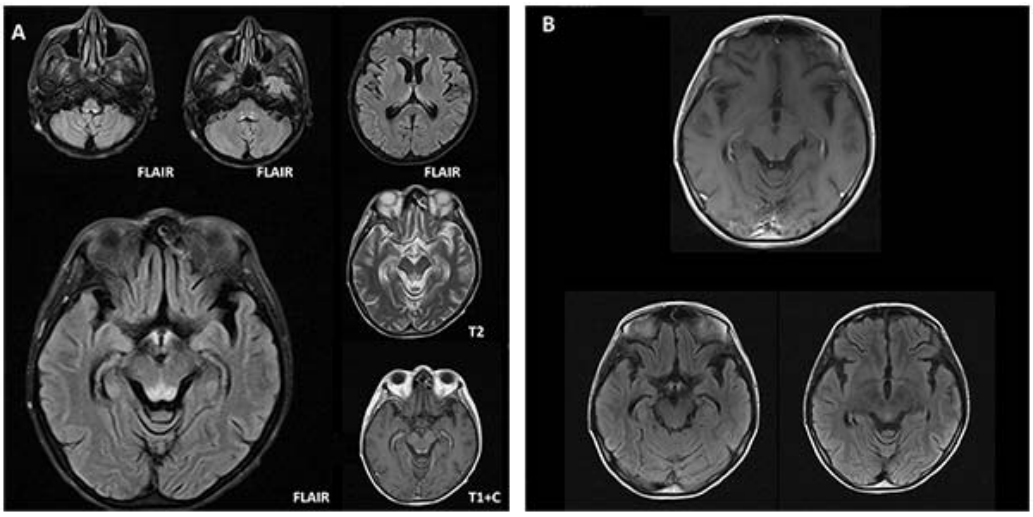


***Figure1A :*** *Bilaterally symmetrical hyperintensities in medial thalami, periaqueductal area, bulbus and mamillary bodies on T2WI and FLAIR . Figure 1B: Follow-up MRI showed resolution of abnormal signals and contrast enhancement .*

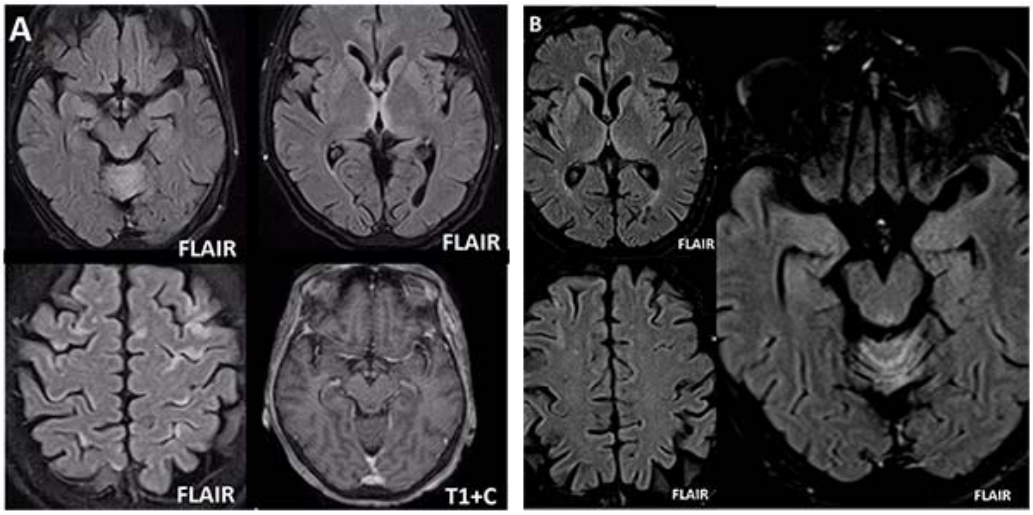


***Figure 2A :*** *Symmetrical hyperintense signals on T2WI and FLAIR in the bilateral ventromedial thalamus, frontobasal region of third ventricle, midbrain, cerebellar vermis, bilateral cortical watershed zones. Figure 2B: Follow-up MRI showed mostly resolution of abnormal signals.*

## CONCLUSION

Twenty-five percent of patients with cancer who are hospitalized have impaired cognition due to infection, metabolic disturbance, organ failure, medication, delirium or metastatic disease (4). WE may develop in patients with cancer because of poor nutritional status, prolonged parenteral nutrition lack of thiamine, administration of glucose-containing fluids, chronic nausea or consumption of thiamine reserves, because of rapid growing cancer like leukemias and sarcomas, malabsorption due to gastrointestinal bypass surgery, low thiamine absorption rate at the mucosal level, and impaired hepatic function (5). According to the EFNS guidelines, cancer is the most common non-alcoholic cause of WE. In the literature, hematologic and gastrointestinal malignancies are the most documented cancers with WE (6).

Due to thiamine's short storage capacity, a notable deficiency can occur within 10 days and more severe deficiency within 21 days if intake is restricted (7). Thiamine supplementation should definitely be added to TPN or the diets of patients with poor oral nutrition. The inadvertent use of glucose-containing fluids should be avoided. In our first case, prolonged hospital stay and parenteral alimentation without thiamine supplementation were considered as predisposing factors. Patient two had a poor diet because of nausea, vomiting, and diarrhea for an extended period.

WE remains a clinical diagnosis that currently gives neuroimaging an important role in the early stage of the disease because of the limitations of determining thiamine deficiency in the laboratory. MRI has 93% specificity and 53% sensitivity to verify the diagnosis of WE (4). Bilateral and symmetric T2WI and FLAIR hyperintensities in the structures around the third ventricle and aqueduct such as the medial thalami, periaqueductal grey matter, mammillary bodies, and the tectal plate of the midbrain are suggested to be sensitive to thiamine deficiency because of their high thiamine-related glucose and oxidative metabolism. Atypical regions are the cerebellum, dentate nuclei, cranial nerve nuclei, red nuclei, caudate nuclei, and the cerebral cortex, which are more common in patients with nonalcoholic WE than alcoholic WE (8-9). Patient two's brain MRI showed cerebellar and cortical involvement concordant with the literature. Contrast enhancement can be seen in about 50% of cases. Patient one's MRI showed contrast enhancement in the midbrain. We performed follow-up MRI for both patients, and each showed great improvement.

In conclusion, WE represents a medical emergency. We propose that all patients with cancer with confusion should be treated with thiamine while undergoing evaluation. Awareness of this condition among physicians and radiologists may reduce morbidity and mortality in WE.

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