

# Clinical Case Report

## Thiamine deficiency in oncology: Clinical insights from two cases of Wernicke's encephalopathy

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### ABSTRACT

Wernicke's encephalopathy (WE) is a neurological disorder primarily caused by thiamine deficiency, typically presenting with malnutrition, confusion or delirium, oculomotor abnormalities (such as nystagmus or ophthalmoplegia), and ataxia. Although commonly associated with alcoholism, WE is frequently observed in oncology patients but is often under-recognised, leading to inadequate diagnosis and treatment. Malnutrition and rapid weight loss in cancer patients can increase the risk of this condition. We report two patients with cancer who presented with significant malnutrition and weight loss, leading to a diagnosis of WE. Both patients were diagnosed based on clinical presentation and magnetic resonance imaging, which is crucial for detecting neurological deficits. Immediate treatment with intravenous thiamine led to a positive clinical response. Early recognition and treatment of WE in oncology patients is essential, as the neurological deficits are potentially reversible. Intravenous thiamine supplementation, and supportive care, can prevent long-term complications.

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### INTRODUCTION

Acute Wernicke's syndrome (WS) typically presents with malnutrition, confusion or delirium, oculomotor abnormalities (such as nystagmus or ophthalmoplegia), and ataxia.<sup>1</sup> Ocular manifestations include lateral rectus palsy, nystagmus, convergence gaze palsy, and may progress to complete external ophthalmoplegia. While sluggish pupillary reactions are common, ptosis and total loss of pupillary response to

light are rare. In some patients, mental symptoms, including progression to coma, may occur without abnormal eye movements, even in pathologically confirmed cases of acute WS.<sup>2</sup>

Brain MRI findings in WS often reveal typical abnormalities, including T2 hyperintense signals and restricted diffusion in the mamillary bodies and thalamus.<sup>3</sup>

Several factors affect thiamine intake and utilization, including chronic alcohol use, malnutrition, gastrointestinal surgical procedures, recurrent vomiting, mucositis, chronic diarrhoea, systemic diseases (e.g. renal diseases, AIDS, chronic infectious febrile diseases, Crohn's disease), and magnesium depletion (e.g. diuretic therapy).<sup>4</sup> Hypermetabolic states—alcohol withdrawal, seizures, infections, critical illness, rapidly growing tumours, diabetes, or dextrose loading—accelerate thiamine utilization. Certain drugs, including metronidazole and 5-fluorouracil (5-FU), may impair thiamine utilization and are recognized risk factors for non-alcoholic WS.<sup>5</sup> Notably, a 'normal' serum thiamine level does not exclude the diagnosis of WS, as it may not reflect intracerebral concentrations.

Patients undergoing cancer-related gastrointestinal procedures or chemotherapy are particularly vulnerable to thiamine deficiency due to reduced intake and availability.<sup>6,7</sup> Chemotherapy agents such as 5-FU, fedratinib, erbulozole, and ifosfamide inhibit thiamine-dependent enzymes involved in carbohydrate metabolism, contributing to cachexia—a syndrome characterized by poor nutrition, systemic inflammation, and muscle wasting.<sup>8,9</sup> Additionally, hyperthyroidism induced by cancer immunotherapies can exacerbate thiamine deficiency through hypermetabolism, while immunotherapy-associated hypothyroidism may lead to deficiency via gastrointestinal malabsorption. Thiamine deficiency may also accelerate in hypermetabolic states or during inflammation associated with cancer.<sup>10</sup>

We report two patients with Wernicke's encephalopathy (WE) due to severe malnutrition and rapid weight loss, underscoring the importance of early clinical evaluation for subclinical thiamine deficiency in cancer patients. Timely diagnosis and intravenous thiamine supplementation are crucial to prevent irreversible neurological deficits, highlighting the need for awareness in oncology care.

### THE CASE

#### Case 1

A 50-year-old woman was admitted with progressive reduced food intake, worsening over the past 2 months, particularly after receiving chemotherapy. Her most recent carboplatin-paclitaxel cycle was completed 10 days before admission. She had not defaecated for a week prior to hospitalization. The patient had a 2-year history of metastatic gastric cancer but no history of smoking, alcohol, or drug use. She appeared malnourished, with a body mass index (BMI) of 16.8 kg/m<sup>2</sup>, and had experienced disorientation, attention deficits, and reduced spontaneous speech for the past 3 days. Bilateral nystagmus was observed on lateral gaze, which began 2 weeks earlier and

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was attributed to ocular ataxia, though no other cerebellar signs were present.

Laboratory tests revealed hypoproteinaemia (3.1 g/dl) and hypokalaemia (2.6 mEq/L), while routine blood work, including complete blood count, liver function tests, and urinalysis, was normal. Brain MRI showed bilateral symmetric diffusion restriction in the thalamus and tectal plate (Fig. 1a,b). Initially, cerebral vascular disease or metastatic brain lesions were considered, but clinical findings combined with characteristic MRI results confirmed a diagnosis of WE secondary to thiamine deficiency.

The patient was treated with intravenous thiamine at a dose of 300 mg, thrice a day for 3 days, followed by 100 mg/day for a week, and transitioned to 100 mg oral thiamine daily. She regained consciousness within a day, her mental status and orientation improved, and she resumed self-feeding. At discharge, her neurological examination was normal, except for mild memory impairment. She was seen at the outpatient clinic 1 month after discharge from the hospital and reported no neurological complaints. Subsequently, she was lost to follow-up.

### Case 2

A 44-year-old male presented with heartburn, significant weight loss (15 kg in 2 months), and 3 days of haematemesis and melaena. Diagnosed with gastric cancer 3 months earlier, he had a 20-year history of smoking and occasional alcohol consumption. He was severely malnourished (BMI 15.6 kg/m<sup>2</sup>), though he had no cerebellar symptoms, mental status changes, or abnormal eye movements. Rectal

examination confirmed melaena. He had low haemoglobin (7.6 g/dl), but routine biochemistry and urine tests were unremarkable.

His oral intake was discontinued, and he received intravenous fluids and a blood transfusion. By the third day of treatment, he developed apathy, disorientation, passivity, hypersomnolence, bilateral gaze limitation, and was minimally responsive to stimuli. Neurological examination revealed an uncooperative finger–nose test. A brain CT obtained on the third day of treatment was unremarkable, but MRI revealed bilateral symmetric hyperintensities in the dorsomedial thalamus and mammillary bodies on T2-weighted imaging (Fig. 1c,d). The combination of clinical presentation, malnourished state, deterioration following dextrose administration, and MRI findings confirmed a diagnosis of WE secondary to thiamine deficiency.

Thiamine replacement therapy was initiated with 500 mg intravenously thrice a day for 3 days, followed by 250 mg/day for 1 week, then transitioned to 100 mg oral thiamine daily. The patient regained consciousness after 3 days with improved mental status and orientation, although mild ataxia was noted during the first week. At discharge, his neurological examination was normal. He had no additional neurological complaints during the follow-up.

### DISCUSSION

Acute WE is treated with high-dose thiamine administration (500 mg intravenously thrice daily for 3 days, followed by once daily for an additional 5 days).<sup>11</sup> In patients at risk for thiamine deficiency (e.g. those with a history of alcoholism or other risk factors for malnutrition), thiamine should be administered prior to glucose in emergency settings to prevent acute WE, as glucose metabolism increases thiamine demand.

In cancer patients, WE can develop post-surgery, during chemotherapy, or at the end of life. Even in newly diagnosed, untreated cancer patients, subclinical thiamine deficiency may be present, highlighting the importance of total nutritional evaluation from the time of diagnosis.<sup>12</sup> We concluded that chronic malnutrition resulting from vomiting and the administration of 5% dextrose was the primary cause of WE in our patients, leading to thiamine deficiency. Therefore, prophylactic thiamine supplementation is crucial for gastric cancer patients from the time of diagnosis. Any malnutrition lasting longer than 4 weeks can deplete thiamine reserves, necessitating thiamine prophylaxis in all cancer patients experiencing nausea, vomiting, decreased appetite, or inadequate oral intake.<sup>13</sup>

The classic triad of ophthalmoplegia, ataxia, and mental disorders is observed in only 16% of patients.<sup>5</sup> Consequently, WE may be misdiagnosed in cancer patients, leading to disease progression due to delayed diagnosis. According to established criteria, WE is diagnosed when two of the following symptoms are present: eye signs, dietary deficiencies, altered mental state, and cerebellar dysfunction. Our patients were diagnosed despite the absence of the complete clinical triad.

Truncal ataxia is seen in more than 80% of patients and can impede standing or walking. Dysarthria and limb ataxia, especially in the arms, are rare.<sup>14</sup> One of our patients had truncal ataxia. There is a correlation between delayed treatment initiation or late diagnosis and the exacerbation of neurological symptoms. Peripheral neuropathy, which occurs to some degree in most patients, can mask ataxia due to resultant weakness. In our

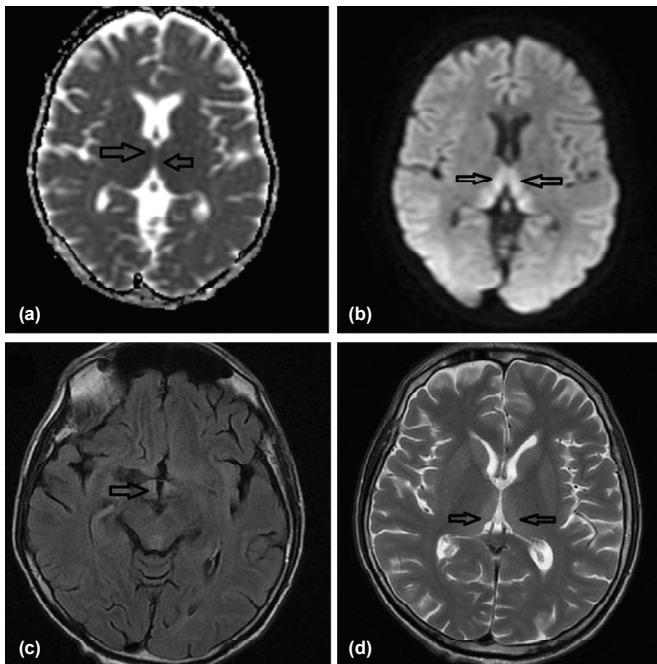


FIG 1. Brain MRI findings: (a) Case 1: MRI axial T2 sequence showing minimal diffusion restriction in the bilateral medial thalamus (black arrows); (b) Case 1: MRI axial diffusion-weighted imaging reveals diffusion brightening in the medial thalamus bilaterally (black arrows); (c) Case 2: MRI T2 sequence displaying signal enhancement in the mammillary bodies (black arrows); (d) Case 2: MRI T2 sequence demonstrating signal enhancement in the bilateral dorsomedial thalamus (black arrows)

patient, ataxia manifested 3 days after the recovery of consciousness. Vestibular caloric test abnormalities are common, with a gradual and often incomplete recovery over several months.

The primary diagnosis of WE is established clinically, but laboratory studies and neuroimaging can also be helpful. Among imaging techniques, MRI is considered the most valuable method for supporting the clinical diagnosis of WE, especially given the low diagnostic sensitivity of CT.<sup>3</sup> MRI findings typically include hyperintense signals in the dorsomedial thalamic nuclei, the third or fourth ventricles, and the periaqueductal grey area. In our patient, CT findings were normal, but MRI revealed characteristic abnormalities. In cancer patients presenting with new neurological symptoms, cerebrovascular events and metastases are often prioritized in differential diagnosis; however, even if CT rules out metastases and infarcts, MRI should be performed for conditions such as WE.

Thiamine plays a critical role in glucose metabolism, and glucose administration may accelerate thiamine consumption, leading to WE. Our patient with gastric bleeding received continuous glucose solutions while oral nutrition was interrupted. Therefore, glucose fluids should be administered alongside thiamine supplementation in malnourished cancer patients.<sup>6</sup>

Some cancer treatments have been linked to WE, attributed to inadequate thiamine supplementation with total parenteral nutrition, the presence of rapidly proliferating neoplastic cells, vomiting, and anorexia. Specific chemotherapy agents, such as 5-FU and ifosfamide, may also contribute to the development of WE.<sup>8</sup> Both patients had a history of 5-FU-based chemotherapy. Furthermore, thiamine-independent chemotherapy-induced central nervous system neurotoxicity can lead to a more dramatic presentation of WE.

Although no published guidelines exist for the treatment of WE in cancer patients, intravenous thiamine supplementation is recommended during the acute phase.<sup>11</sup> Our patients had marked improvement in mental status, though ataxia persisted

in one patient at discharge. We report these patients to raise awareness of malnutrition in cancer patients and to emphasize the importance of early diagnosis and treatment once WE develops.

*Conflicts of interest.* None declared

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