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## **Case Report**

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#### **Keywords:**

Cancer; Suicide; Thiamine; Wernicke encephalopathy; Major depression

**Corresponding author:** Mayumi Ishida; Email: mayumi\_i@saitama-med.ac.jp

# What can cause cancer patients to attempt suicide? Thiamine deficiency mimicking the symptoms of major depressive disorder

Mayumi Ishida, с.Р., РН.D.<sup>1</sup> (), Sho Sato, м.D., РН.D.<sup>2</sup>, Izumi Sato, м.Р.Н., РН.D.<sup>3</sup>, Akira Yoshioka, м.D., РН.D.<sup>4</sup>, Nozomu Uchida, м.D.<sup>5</sup> (), Naoki Mizunuma, атту.<sup>6</sup>, Kosei Hasegawa, м.D., РН.D.<sup>2</sup> and Hideki Onishi, м.D., РН.D.<sup>1</sup> ()

<sup>1</sup>Department of Psycho-oncology, Saitama Medical University International Medical Center, Saitama, Japan;
 <sup>2</sup>Department of Gynecologic Oncology, Saitama Medical University International Medical Center, Saitama, Japan;
 <sup>3</sup>Department of Clinical Epidemiology, Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, Japan;
 <sup>4</sup>Department of Medical Oncology and Palliative Care, Mitsubishi Kyoto Hospital, Kyoto, Japan;
 <sup>5</sup>Department of General Medicine, Ogano Town Central Hospital, Saitama, Japan and <sup>6</sup>Tokyo Kagurazaka Law Office, Tokyo, Japan

#### Abstract

**Objectives.** Thiamine deficiency (TD) presents with various physical and psychiatric symptoms, but no cases with depression-like symptoms have been reported.

**Methods.** We report a patient with cancer who appeared to attempt suicide as a consequence of depressive mood likely related to TD.

**Results.** The patient was a 58-year-old woman diagnosed with recurrent endometrial cancer, with lung metastasis and pelvic dissemination. The patient apparently attempted suicide was referred to the psycho-oncology department.

At the time of the examination, major depressive disorder was suspected based on her mental symptoms, but when thiamine was administered intravenously in response to her poor dietary intake, her palpitations, dyspnea, anorexia, and insomnia improved, and her suicidal ideation disappeared at her reexamination 1 hour later after thiamine administration.

**Significance of results.** It is likely that the observed palpitations, dyspnea, anorexia, and insomnia, as well as the severe depression and the attempted suicide, which were thought to be physical symptoms associated with depression, were actually related to TD. Suicidal ideation and attempted suicide are conspicuous as psychiatric symptoms. However, in such cases, rather than simply starting treatment for depression, it is necessary to consider reversible TD as a cause of these symptoms and perform differential diagnosis to confirm the physical illness.

## Introduction

Thiamine, in its biologically active form of thiamine pyrophosphate, is an essential coenzyme for oxidative cellular metabolism (Sechi et al. 2016a). However, as humans cannot synthesize thiamine in the body, they rely on external sources. Moreover, the physiological stores are small, and thiamine deficiency (TD) may occur if a loss of appetite continues for 2–3 weeks (Sechi et al. 2016a). Wernicke encephalopathy (WE) is well known as a serious disease caused by TD. If left untreated, Korsakoff syndrome may develop, resulting in irreversible brain damage (Sechi and Serra 2007). The treatment of TD is preferably the parenteral administration of thiamine, and early detection and treatment allows the disease to be resolved without sequelae. However, the neuropsychiatric symptoms exhibited by TD patients are nonspecific, and cases in which the symptoms are mild or vague often go undiagnosed (Fozi et al. 2006; Harper et al. 1986; Onishi et al. 2019b). At present, the most useful diagnostic tool for TD is clinical suspicion (Sechi and Serra 2007). For this reason, it is essential that we increase our knowledge of the classical features of TD as well as of other possible, more uncommon symptoms.

Herein, we report a case of TD mimicking major depressive disorder (MDD) in which the patient showed severe mental symptoms including attempted suicide, depression, low motivation, and frustration.

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## Case report

A gynecological oncologist referred a 58-year-old female patient with endometrial cancer to the psycho-oncology department.



Three years earlier, the patient visited an emergency center due to massive genital bleeding. As a result of detailed examination in the gynecology department, she was suspected as Stage IA endometrial cancer and underwent a total abdominal hysterectomy and bilateral salpingo-oophorectomy. The patient was diagnosed with endometrial cancer, Stage IA (pT1aNXM0). She was followed up regularly by a gynecological oncologist.

Three months before her visit to our clinic, lung metastasis and pelvic dissemination were confirmed by computed tomography/magnetic resonance imaging, and recurrence was diagnosed.

Two months before her visit, at the start of the first course of docetaxel and carboplatin (DC) therapy, the patient's physical findings were as follows: height, 153 cm; weight, 45 kg; and body mass index (BMI), 19.22 kg/m<sup>2</sup>.

A few days after the start of DC administration, the patient experienced a loss of appetite and vomiting (about 10 times a day) that persisted for about a week, but she gradually recovered. The second course of treatment was completed without any symptoms of loss of appetite or vomiting. Two weeks before her visit, during the third course of treatment, the patient experienced vomiting about 5 times a day from the day after administration, with marked loss of appetite and dysgeusia, and she took only 1 mouthful of fruit and ice cream a day for about a week, leading to increased fatigue.

Ten days before her visit, the patient experienced severe nausea and 15 mg of metoclopramide was additionally administered.

Seven days before her visit, she visited the gynecology department for a special examination. Her notebook, in which she recorded her physical symptoms and feelings, contained the following comments describing her anxiety regarding future treatment: "I have no place to put my feelings," "I am causing trouble to everyone because of my weakness," "I can't enjoy the things I used to enjoy." At her request, she was referred to the psycho-oncology department.

On her first visit to the psycho-oncology department, she appeared restless. During the examination, she couldn't sit calmly and remained standing in the room while responding to inquiries. She stated that "I'm trembling," "I have heart palpitations," and "Today is the hardest" in quick succession. Then, while gesturing with her hands around her throat, she complained, "I choked myself with both hands."

Further interviews were recommended, and a depressed mood and decreased motivation were observed. The patient's appetite decreased to about 10% of normal, and she slept poorly, waking every hour and experiencing nightmares. The patient was observed to demonstrate signs of frustration, such as feeling trapped and restless, and she also complained of general malaise, difficulty in concentrating, and feelings of guilt. These symptoms caused her clinically significant distress.

Neurologically, bilateral tremors were present, but no ataxia, ocular symptoms, or decreased level of consciousness were noted. She had noted "dizziness" in the notebook and there were some irregularities in her writing.

Physically, she weighed 43 kg (BMI,  $18.37 \text{ kg/m}^2$ ), with a body temperature of  $36.5^{\circ}$ C, blood pressure of 114/80 mm Hg, pulse of 88 bpm, and oxygen saturation of 98%. No special features were observed in her blood and biochemical data (Table 1).

She had no history of depression or psychiatric illness, nor was there a history of alcohol or substance abuse. Personalitywise, she was earnest, warm-hearted, and deeply trusted by those around her.

The above mental and physical symptoms met the list of A items as symptoms of depression under the diagnostic criteria of

Table 1. Patient blood and biochemical findings

Biochemical findings           Albumin         3.8 L         4.10–5.10 g/dL           Creatine kinase         99         41.00–153.00 U/L           AST         22         13.00–30.00 U/L           ALT         23         7.00–23.00 U/L           Lactate dehydrogenase (LD_IFCC)         278 H         124.00–222.00 U/L           Alkaline phosphatase (LD_FCC)         66         38.00–113.00 U/L           Alkaline phosphatase (JSCC converted value)         187         104.00–338.00 U/L           YGTP         49 H         9.00–32.00 U/L           Creatinine         0.58         0.46–0.79 mg/dL           eGFR (Female)         81.1         mL/min/1           Uric acid         3.80         2.60–5.50 mg/dL           Blood glucose         130 H         73.00–109.00 mg/dL           Hemoglobin A1c         5.7         4.90–6.00 %NGSP           Sodium         141         138.00–145.00 mmol/L           Chloride         104         101.00–108.00 mmol/L           Potassium         3.4 L         3.60–4.80 mmol/L           Calcium         9.1         8.80–10.10 mg/dL           Blood findings         3.00 L         3.86–4.92 × 1 million/µ           Hematocrit         2.68 L         3.30–8.6	Item	Results Reference range							
Creatine kinase         99         41.00-153.00 U/L           AST         22         13.00-30.00 U/L           ALT         23         7.00-23.00 U/L           Lactate dehydrogenase (LD_IFCC)         278 H         124.00-222.00 U/L           Alkaline phosphatase (ALP_IFCC)         66         38.00-113.00 U/L           Alkaline phosphatase (JSCC converted value)         187         104.00-338.00 U/L           YGTP         49 H         9.00-32.00 U/L           Creatinine         0.58         0.46-0.79 mg/dL           eGFR (Female)         81.1         mL/min/1           Uric acid         3.80         2.60-5.50 mg/dL           Blood glucose         130 H         73.00-109.00 mg/dL           Hemoglobin A1c         5.7         4.90-6.00 %NGSP           Sodium         141         138.00-145.00 mmol/L           Chloride         104         101.00-108.00 mmol/L           Potassium         3.4 L         3.60-4.80 mmol/L           Blood findings         1         1.60-14.80 g/dL           Blood findings         3.00 L         3.86-4.92 × 1 million/μ           Hemoglobin content         10 L         11.60-14.80 g/dL           Hematocrit         29.1 L         35.10-44.40%           <	Biochemical findings								
AST         22         13.00-30.00 U/L           ALT         23 $7.00-23.00$ U/L           Lactate dehydrogenase (LD_IFCC)         278 H $124.00-222.00$ U/L           Alkaline phosphatase (LD_IFCC)         66 $38.00-113.00$ U/L           Alkaline phosphatase (JSCC converted value)         187 $104.00-338.00$ U/L $\gamma$ GTP         49 H $9.00-32.00$ U/L           Creatinine         0.58 $0.46-0.79$ mg/dL           eGFR (Female)         81.1         mL/min/1           Uric acid $3.80$ $2.60-5.50$ mg/dL           Blood glucose         130 H $73.00-109.00$ mg/dL           Hemoglobin A1c $5.7$ $4.90-6.00$ %NGSP           Sodium         141 $138.00-145.00$ mmol/L           Chloride         104 $101.00-108.00$ mmol/L           Chloride         104 $101.00-108.00$ mmol/L           Potassium $3.4$ L $3.60-4.80$ mmol/L           Blood findings         130 H $3.30-8.60 \times 1000/\mu$ Blood count $2.68$ L $3.30-8.60 \times 1000/\mu$ White blood cell count $3.00$ L $3.86-4.92 \times 1$ million/ $\mu$ Hematocrit $29.1$ L	Albumin	3.8 L	4.10-5.10 g/dL						
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(LD_IFCC)       Alkaline phosphatase       66 $38.00-113.00 \text{ U/L}$ Alkaline phosphatase       187 $104.00-338.00 \text{ U/L}$ (JSCC converted value)       187 $104.00-338.00 \text{ U/L}$ $\gamma$ (GTP       49 H $9.00-32.00 \text{ U/L}$ Creatinine $0.58$ $0.46-0.79 \text{ mg/dL}$ eGFR (Female) $81.1$ mL/min/1         Uric acid $3.80$ $2.60-5.50 \text{ mg/dL}$ Blood glucose $130 \text{ H}$ $73.00-109.00 \text{ mg/dL}$ Hemoglobin A1c $5.7$ $4.90-6.00 \text{ %NGSP}$ Sodium       141 $138.00-145.00 \text{ mmol/L}$ Chloride $104$ $101.00-108.00 \text{ mmol/L}$ Potassium $3.4 \text{ L}$ $3.60-4.80 \text{ mmol/L}$ Calcium $9.1$ $8.80-10.10 \text{ mg/dL}$ Total bilirubin $0.2 \text{ L}$ $0.40-1.50 \text{ mg/dL}$ Blood count $2.68 \text{ L}$ $3.30-8.60 \times 1000/\mu$ Red blood cell count $2.68 \text{ L}$ $3.30-8.60 \times 1000/\mu$ Hematocrit $29.1 \text{ L}$ $35.10-44.40\%$ Mean corpuscular $97$ $83.60-98.20 \text{ fL}$ volume $33.3 \text{ H}$ $27.50-3$	ALT	23 7.00–23.00 U/L							
(ALP_IFCC)         Alkaline phosphatase (JSCC converted value)       187       104.00-338.00 U/L $\gamma$ GTP       49 H       9.00-32.00 U/L         Creatinine       0.58       0.46-0.79 mg/dL         eGFR (Female)       81.1       mL/min/1         Uric acid       3.80       2.60-5.50 mg/dL         Blood glucose       130 H       73.00-109.00 mg/dL         Hemoglobin A1c       5.7       4.90-6.00 %NGSP         Sodium       141       138.00-145.00 mmol/L         Chloride       104       101.00-108.00 mmol/L         Potassium       3.4 L       3.60-4.80 mmol/L         Calcium       9.1       8.80-10.10 mg/dL         Total bilirubin       0.2 L       0.40-1.50 mg/dL         Blood count       2.68 L       3.30-8.60 × 1000/µ         White blood cell count       2.68 L       3.30-8.60 × 1000/µ         Red blood cell count       3.00 L       3.86-4.92 × 1 million/µ         Hematocrit       29.1 L       35.10-44.40%         Mean corpuscular       97       83.60-98.20 fL         volume       33.3 H       27.50-33.20 pg         Mean corpuscular       34.4       31.70-35.30 g/dL         Iar hemoglobin content       34.4 <t< td=""><td></td><td>278 H</td><td>124.00-222.00 U/L</td></t<>		278 H	124.00-222.00 U/L						
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Blood findingsBlood countWhite blood cell count2.68 L3.30-8.60 × 1000/μRed blood cell count3.00 L3.86-4.92 × 1 million/μHemoglobin content10 L10 L11.60-14.80 g/dLHematocrit29.1 L35.10-44.40%Mean corpuscular volume9783.60-98.20 fLMean corpuscular hemoglobin content33.3 H27.50-33.20 pgMean corpuscular hemoglobin concentration34.431.70-35.30 g/dL	Calcium	9.1	8.80-10.10 mg/dL						
Blood count         White blood cell count       2.68 L       3.30-8.60 × 1000/μ         Red blood cell count       3.00 L       3.86-4.92 × 1 million/μ         Hemoglobin content       10 L       11.60-14.80 g/dL         Hematocrit       29.1 L       35.10-44.40%         Mean corpuscular volume       97       83.60-98.20 fL         Mean corpuscular hemoglobin content       33.3 H       27.50-33.20 pg         Mean corpuscular concentration       34.4       31.70-35.30 g/dL	Total bilirubin	0.2 L	0.40-1.50 mg/dL						
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Hemoglobin content10 L11.60–14.80 g/dLHematocrit29.1 L35.10–44.40%Mean corpuscular volume9783.60–98.20 fLMean corpuscular hemoglobin content33.3 H27.50–33.20 pgMean corpuscu- lar hemoglobin concentration34.431.70–35.30 g/dL	White blood cell count	2.68 L	$3.30-8.60 \times 1000/\mu$						
Hematocrit29.1 L35.10-44.40%Mean corpuscular volume9783.60-98.20 fLMean corpuscular hemoglobin content33.3 H27.50-33.20 pgMean corpuscu- lar hemoglobin concentration34.431.70-35.30 g/dL	Red blood cell count	3.00 L	3.86–4.92 × 1 million/ $\mu$						
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hemoglobin content Mean corpuscu- lar hemoglobin concentration	•	97	83.60-98.20 fL						
lar hemoglobin concentration	-	33.3 H	27.50-33.20 pg						
	lar hemoglobin	34.4	31.70-35.30 g/dL						
Platelet count 194 $158.00-348.00 \times 1000/\mu$	Platelet count	194	158.00–348.00 × 1000/ $\mu$						

Abbreviations: AST-aspartate aminotransferase; ALT-alanine aminotransferase.

Table 2. Vitamin levels at the time of psychiatric consultation

Item	Results	Reference range		
Vitamin B1	14	24.0-66.0 ng/mL		
Vitamin B12	339	180.0-914.0 pg/mL		

the Diagnostic and Statistical Manual of Mental Disorders 5th edition (American Psychiatric Association 2013). A 2-week period of decreased appetite is one of the diagnostic criteria for depression. However, this also corresponds to the period during which

Table 3. Comparison of the psychiatric symptoms before and after intravenous administration of thiamine

DSM-5 (Depressive symptoms)	X – 7 days	Х	X + 1 hour after VB1 administration	X + 1  day	X + 4  days	X + 7 days
1. Depressed mood	+	+	_	-	-	-
2. Loss of interest/pleasure	+	+	-	-	-	-
3. Weight loss or gain	+	+	_	-	-	-
4. Insomnia or hypersomnia	+	+	NA	-	-	-
5. Psychomotor agitation or retardation	+	+	_	-	-	-
6. Fatigue	+	+	-	-	-	-
7. Feeling worthless or excessive/inappropriate guilt	+	+	-	-	-	-
8. Decreased concentration	+	+	_	-	-	-
9. Thoughts of death/suicide	+	+	_	-	-	-

TD might develop (Sechi et al. 2016a), so we also suspected TD and intravenously administered 200 mg of thiamine. When the patient was examined again after 1 hour, there was a significant change in symptoms, with the patient stating, "I feel better," "I no longer have heart palpitations," and "the feeling of wanting to die has disappeared." Thereafter, her appetite improved rapidly and, after the examination, she ate a normal amount of food at a restaurant with her family and went home.

Oral administration of mirtazapine 15 mg and aripiprazole 3 mg before bedtime was started from that day. On the next day, she reported that, "I was able to sleep for nine hours," "I no longer have dizziness, lightheadedness, or headaches," and "I have a strong desire to undergo cancer treatment." She also reported that she no longer experienced tremors. According to the patient, her appetite improved thereafter, and she ate hamburgers with her family even before examinations.

Four days later, her weight had increased by 2 kg, and she declared that, "I don't want to die now. I want to live." Her family also reported that she had increased her food intake.

Five days later, the patient's serum thiamine concentration was found to be 14 ng/mL (reference range: 24–66 ng/mL), which was abnormally low (Table 2).

Based on the above, this patient was diagnosed with TD, and oral administration of thiamine 100 mg was continued. No recurrence of similar symptoms has since been observed.

#### Discussion

We experienced a case in whom depression was initially suspected as the cause of severe psychiatric symptoms including attempted suicide and frustration. However, in consideration of the possibility of TD, she was intravenously administered thiamine and her subjective mental symptoms almost disappeared before the start of treatment for depression.

The cause of TD in this case was understood to be a reduced appetite (Sechi et al. 2016a), but the possibility of chemotherapy-induced TD cannot be ruled out (Sechi et al. 2016b).

When we tracked the time course of each psychiatric symptom in this case, suicidal ideation was observed to disappear on the day of thiamine administration at the outpatient clinic, and many symptoms such as loss of appetite also disappeared (Table 3). This is consistent with the report that TD is a risk factor for developing neuropsychiatric symptoms (Iimura et al. 2021).

Considering the symptoms and course, treatment for TD was the most urgent response, and it is thought that TD caused these symptoms mimicking MDD. Previous reports have also pointed out the relationship between decreased appetite due to depression and vitamin deficiency (Oudman et al. 2021), and caution should be exercised in differentiating comorbid depression and depressive states from TD.

The failure to consider the possibility of TD in cases like this, resulting in treatment with antidepressants alone, can lead to Korsakoff syndrome, an irreversible brain disorder.

At the examination, no disturbed consciousness was observed in this case. However, as delirium tends to show diurnal fluctuations, it is possible that her consciousness was disturbed at the time of her attempted suicide.

In addition, the administration of antidepressants was started even after symptoms improved in response to the administration of thiamine on an outpatient basis. As depression also shows diurnal fluctuations, it is possible that the symptoms of "suicidal ideation" were more marked at the time the suicide attempt was made. It is also possible for symptoms to become stronger again after examination; therefore, there is no leeway for a wait-and-see approach, and we believe that starting treatment with the prescription of antidepressants is important for life-threatening risk avoidance.

In conclusion, attempted suicide is a very serious action resulting from psychiatric symptoms. However, in oncological settings, as in this case, we should consider not only depression but also the possibility of TD as a physical disease. TD is a potentially iatrogenic condition and fatal if overlooked, but is reversible if detected early. Appropriate diagnosis and treatment, including early detection and differential diagnosis, are always important.

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