Development of Wernicke-Korsakoff Syndrome After Long Intervals Following Gastrectomy

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Background: Surgical exclusion of portions of the gastrointestinal tract is a predisposing risk factor for the development of Wernicke-Korsakoff syndrome. When this disease occurs, it is usually within weeks after the gastrointestinal surgery. However, it is not well known that Wernicke-Korsakoff syndrome may occur after a long latent interval following gastrectomy.

Setting: A research-oriented hospital.

Patients: Three patients without a history of alcoholism or dietary deprivation developed Wernicke-Korsakoff syndrome 2 to 20 years after undergoing gastrectomy. In these patients, minor changes in dietary habit led to the development of Wernicke-Korsakoff syndrome.

Conclusions: In addition to a long-standing latent deficiency in thiamin levels due to defective absorption following gastrectomy or gastrojejunostomy, other minor factors that may influence the intake of thiamin and the need for thiamin in subjects who have undergone gastrectomy may cause a state of thiamin deficiency resulting in Wernicke-Korsakoff syndrome. Results from our study indicate that the following measures are mandatory: educating patients about proper dietary habits, carefully monitoring their thiamin intake, recognizing Wernicke-Korsakoff syndrome early, and treating it immediately with appropriate measures.

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REPORT OF CASES

PATIENT 1

A 51-year-old male truck driver with no history of alcoholism was referred to our hospital on October 26, 1995, because of behavioral derangement and an unsteady gait that had lasted for 8 days. The patient had undergone a total resection of the stomach and gastrojejunostomy because of gastric adenocarcinoma in 1990. After the surgery, he remained in good health and had regularly taken a vitamin supplement (10 mg/d of thiamin and 13 µg/d of...
cycocobalamin). He experienced an episode of confusion in April 1995, which subsided after a few days with a residual retrograde amnesia in relation to the preceding 10 days. On October 5, 1995, 3 weeks after the patient had discontinued taking the vitamin supplement, he became confused and developed gait ataxia. He was treated with oral vitamin B complex tablets prescribed by a physician. Serum levels of thiamin and vitamin B12 determined prior to the treatment were 65 nmol/L (normal range, 77-199 nmol/L) and 314 pmol/L (normal range, 184-692 pmol/L), respectively.

On admission, the patient was confused and disoriented. His weight was 38.6 kg and his height was 159 cm. A neurologic examination revealed gaze-evoked horizontal nystagmus, ataxia, and hyporeflexia at the ankles. Anterograde amnesia and retrograde memory loss in relation to the preceding several years were apparent. The patient's verbal response included many confabulations. Two months later, the patient scored a 22 on the Mini-Mental State Examination. A routine laboratory examination revealed mild macrocytic anemia (red blood cell count, 3.16×10^12/L; hemoglobin, 110 g/L; and hematocrit, 0.33). Results from a lumbar puncture revealed normal cerebrospinal fluid findings. An electroencephalogram showed diffuse slow activities. Motor and sensory nerve conduction velocities were within normal ranges. Cranial magnetic resonance imaging scans demonstrated mild brain atrophy but no focal abnormality. There was no evidence of cancer recurrence. The patient's episodic memory was not functioning properly, and he had retrograde amnesia relative to the 2-year period prior to the onset of his condition. The patient was disoriented in space and time, and his confabulations were remarkable. On the Wechsler Memory Scale–Revised, the patient scored a 61 on the general memory index, 61 on the verbal memory index, 76 on the visual memory index, and 57 on the delayed recall index. His intellectual function had declined to a subnormal level; he had a verbal IQ of 81 and a performance IQ of 77 on the Wechsler Adult Intelligence Scale–Revised.

The patient was diagnosed as having Wernicke encephalopathy. Following treatment with intravenous high-dose thiamin for 2 weeks and then oral thiamin, he gradually recovered from hyporeflexia and dysesthesia. Although the patient's disorientation and confabulation became less severe 2 months later, his amnesia remained unchanged.

PATIENT 3

A 60-year-old businessman with no history of alcoholism was referred to our hospital on July 8, 1997, because of the onset of an acute memory impairment 11 days earlier. The patient had undergone a partial gastrectomy and gastrojejunostomy in July 1995 for gastric adenocarcinoma and had been in good health thereafter. Two weeks before the onset of the patient's memory problems, he had an upper respiratory tract infection and poor appetite. A family physician had given him a single dose of vitamin B complex (containing 50 mg of thiamin hydrochloride) with fluid under the suspected diagnosis of mild undernourishment and dehydration.

On admission, the patient was alert but severely amnestic and disoriented. Some confabulations were noted. The results of the general physical examination were unremarkable. The patient's weight was 44.0 kg and his height was 151 cm. The results of his general physical examination were not remarkable. A neurologic examination revealed hyporeflexia at the ankles, dysesthesia on the feet, and truncal ataxia. There was no evidence of oculomotor disturbance or nystagmus. The patient scored a 21 on the Mini-Mental State Examination. Serum levels of thiamin and vitamin B12 were 65 nmol/L and 314 pmol/L, respectively. Results from a routine examination of blood and urine were otherwise normal. A lumbar puncture yielded normal cerebrospinal fluid findings. An electroencephalogram showed diffuse theta activities. Motor and sensory nerve conduction velocities were within normal ranges. Cranial magnetic resonance imaging scans demonstrated mild brain atrophy but no focal abnormality. The patient's episodic memory was not functioning properly, and he had retrograde amnesia relative to the 2-year period prior to the onset of his condition. The patient was disoriented in space and time, and his confabulations were remarkable. On the Wechsler Memory Scale–Revised, the patient scored a 61 on the general memory index, 61 on the verbal memory index, 76 on the visual memory index, and 57 on the delayed recall index. His intellectual function had declined to a subnormal level; he had a verbal IQ of 81 and a performance IQ of 77 on the Wechsler Adult Intelligence Scale–Revised.

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PATIENT 2

A 65-year-old male factory worker was admitted to our hospital on May 7, 1996, because of memory problems and an unsteady gait that had developed 1 month earlier. The patient had had a partial gastrectomy and gastrojejunostomy in 1976 because of gastric adenocarcinoma and was in good health thereafter. He suffered from anorexia and invertebrate insomnia in March 1996, and his daily alcohol consumption had increased to twice his habitual drinking level for 30 years of 400 mL of wine per day. One month later, the patient became confused, developed an unsteady gait, and was treated under a diagnosis of depression. After he ceased drinking, the patient became less confused and the disturbance in his gait improved slightly, but a problem with his memory became apparent.

On admission, the patient was alert. His weight was 44.0 kg and his height was 151 cm. The results of his general physical examination were not remarkable. A neurologic examination revealed hyporeflexia at the ankles, dysesthesia on the feet, and truncal ataxia. There was no evidence of oculomotor disturbance or nystagmus. The patient scored a 21 on the Mini-Mental State Examination. Serum levels of thiamin and vitamin B12 were 65 nmol/L and 314 pmol/L, respectively. Results from a routine examination of blood and urine were otherwise normal. A lumbar puncture yielded normal cerebrospinal fluid findings. An electroencephalogram showed diffuse theta activities. Motor and sensory nerve conduction velocities were within normal ranges. Cranial magnetic resonance imaging scans demonstrated mild brain atrophy but no focal abnormality. A 99mTc-ethyl cyaicobalamine. He experienced an episode of confusion in April 1995, which subsided after a few days with a residual retrograde amnesia in relation to the preceding 10 days. On October 5, 1995, 3 weeks after the patient had discontinued taking the vitamin supplement, he became confused and developed gait ataxia. He was treated with oral vitamin B complex tablets prescribed by a physician. Serum levels of thiamin and vitamin B12 determined prior to the treatment were 65 nmol/L (normal range, 77-199 nmol/L) and 319 pmol/L (normal range, 184-692 pmol/L), respectively.

On admission, the patient was confused and disoriented. His weight was 38.6 kg and his height was 159 cm. A neurologic examination revealed gaze-evoked horizontal nystagmus, ataxia, and hyporeflexia at the ankles. Anterograde amnesia and retrograde memory loss in relation to the preceding several years were apparent. The patient's verbal response included many confabulations. Two months later, the patient scored a 22 on the Mini-Mental State Examination. A routine laboratory examination revealed mild macrocytic anemia (red blood cell count, 3.16×10^12/L; hemoglobin, 110 g/L; and hematocrit, 0.33). Results from a lumbar puncture revealed normal cerebrospinal fluid findings. An electroencephalogram showed diffuse slow activities. Motor and sensory nerve conduction velocities were within normal ranges. Cranial magnetic resonance imaging scans demonstrated mild brain atrophy but no focal abnormality. There was no evidence of cancer recurrence. The patient was immediately treated with intravenous high-dose thiamin and cyanocobalamin, followed by oral vitamin B complex tablets. Soon after treatment was initiated, the patient's confusion disappeared and his nystagmus and ataxia gradually subsided. However, there was only a slight improvement in his memory and disorientation. Two months later, the patient scored less than 50 on the general memory index of the Wechsler Memory Scale–Revised, 53 on the verbal memory index, 64 on the visual memory index, and less than 50 on the delayed recall index. There was no improvement in his retrograde amnesia. The patient's intellectual function had declined to a subnormal level; he had a verbal IQ of 89 and a performance IQ of 78 on the Wechsler Adult Intelligence Scale–Revised. There was a mild decrease in regional cerebral blood flow and the oxygen metabolic ratio in the patient's frontal lobes, as determined by a positron emission tomographic scan and the oxygen 15-labeled gas inhalation steady state method.
In our 3 patients, the onset of acute characteristic signs and symptoms, a low serum level of thiamin (documented in 2 patients), and the patients’ responses to thiamin supported the diagnosis of Wernicke-Korsakoff syndrome. The marked disparity between the memory quotients and general IQs of our patients also indicated the Korsakoff amnestic disorder. 

Neuroimaging studies ruled out other causes, including vascular and degenerative diseases. Although a decreased serum vitamin B<sub>12</sub> concentration and macrocytic anemia were found in patient 1, it was unlikely that a vitamin B<sub>12</sub> deficiency had caused his neurologic manifestations.

Although Wernicke-Korsakoff syndrome is most commonly associated with chronic alcoholism, it has also been recognized to occur with a variety of abnormalities of the gastrointestinal tract. 1,2 It generally develops weeks after gastric plication for morbid obesity 4-5 or gastrectomy for neoplasm 11 in association with starvation, 12 anorexia, 13 recurrent vomiting, 8,9,14 and/or prolonged parenteral feeding. 15 However, in our patients, Wernicke-Korsakoff syndrome occurred after long latent intervals ranging from 2 to 20 years following gastrectomy or gastrojejunostomy. Neither chronic anorexia, restriction of diet, nor recurrent vomiting was associated with the development of Wernicke-Korsakoff syndrome. The alcohol consumption of our patients was not excessive and their diet was appropriate and balanced. Although a single case report of a similar condition appeared in the Japanese medical literature, 16 no report was found in the Western literature.

For each of our patients, we noted the following trivial predisposing events that occurred just before the onset of Wernicke-Korsakoff syndrome: patient 1 had discontinued taking vitamin supplements 3 weeks prior to onset; patient 2 had increased alcohol consumption and experienced a loss of appetite 1 month prior to onset; and patient 3 had developed an upper respiratory tract infection and a poor appetite 2 weeks prior to onset. Each of these minor factors alone does not generally cause a deficiency in thiamin levels. A gastrojejunostomy makes the foodstuff passage circumvent the duodenum, where the absorption of thiamin mainly takes place. In our patients, minimal levels of thiamin were barely maintained for long periods after surgery. All of our patients showed signs of mild polyneuropathy, including diminished ankle jerks and paresthesia of the feet, suggesting a marginal malnutrition prior to surgery, since long survival after gastrectomy is often associated with a nutritional polyneuropathy. 12 We may better understand the clinical form of Wernicke-Korsakoff syndrome when minor episodes comprising combinations of such subtle features are reported in other patients. A decrease in thiamin supply, an increase in the need for thiamin, and inefficient absorption promote a state of thiamin deficiency. Aging, which reportedly increases the need for thiamin, 3 may contribute to the development of a relative thiamine deficiency. In addition, the Japanese diet consists mainly of highly milled rice, which has an excessive proportion of carbohydrates relative to the supply of thiamin and thus may favor the development of a state of thiamin deficiency. In each of our patients, a relatively mild increase in thiamin deficiency was sufficient to convert a mild chronic athiaminotic state to an acute athiaminotic state, (ie, Wernicke-Korsakoff syndrome).

Among our patients, one (patient 1) had a premonitory transient episode of confusion and residual retrograde amnesia, which were disregarded by the patient’s physician. The initial treatment of all our patients was inadequate. Early recognition of Wernicke-Korsakoff syndrome is crucial, considering the poor prognosis without appropriate treatment. A delay of treatment can cause death or serious permanent deficits. It should be recognized that undergoing gastrectomy or gastrojejunostomy is not an uncommon risk factor for Wernicke-Korsakoff syndrome. Minor factors that may influence the intake of thiamin and the need for thiamin in individuals who have undergone gastrectomy or gastrojejunostomy can cause a state of thiamin deficiency resulting in this syndrome. Moreover, it is important to educate patients who have undergone gastrectomy in proper dietary habits, carefully monitor their thiamin intake, recognize Wernicke-Korsakoff syndrome early, and treat it immediately with appropriate measures.

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