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**Case Report**

# Wernicke's Encephalopathy after Gastrectomy and Adjuvant Chemotherapy Using S-1 for Gastric cancer : Report of a Case

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**SUMMARY**

Wernicke's encephalopathy is a disease usually related to chronic alcoholism. We reported a case of Wernicke's encephalopathy after distal gastrectomy and chemotherapy using S-1 despite of no history of alcoholism. A 58-year-old woman underwent distal gastrectomy for gastric carcinoma in February, 2005. She received adjuvant chemotherapy using S-1, since histological examination of the removal specimens showed regional lymph nodes metastasis. After this therapy, she rapidly developed diplopia, ataxia and disturbance of consciousness. Although brain CT and the routine laboratory data showed no abnormal changes, brain MRI showed a symmetrical high-intensity area in the third ventricle and periaqueductal regions ; this was characteristic of Wernicke's encephalopathy. She was immediately treated with thiamine, and recovered consciousness within a few hours. S-1 based on 5-fluorouracil (5-FU) which reduced the thiamine levels in the patient, may have worsened the thiamine deficiency caused by distal gastorectomy. Therefore, clinicians should pay attention to suspicious symptoms of thiamine deficiency in patients who have undergone gastrectomy, particularly those who receive adjuvant chemotherapy with S-1 or 5-FU.

**Key Words** : Wernicke's Encephalopathy, gastrectomy, S-1 Chemotherapy

## INTRODUCTION

Wernicke's encephalopathy caused by thiamine deficiency is most commonly seen in alcoholic patients. Several cases have recently been described as Wernicke's encephalopathy after gastric restrictive surgery in patients with morbid obesity, and after gastrectomy or receiving 5- fluorouracil (5-FU) chemotherapy for gastric carcinoma[1～5].

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We report a case of Wernicke's encephalopathy after astrectomy and adjuvant chemotherapy using S-1 for gastric cancer.

## CASE REPORT

A 58-year-old woman was referred to our hospital with severe anemia and epigastralgia, in January 2005. Other laboratory data on admission were unremarkable. Serum carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) levels were within the normal ranges. Upper gastrointestinal endoscopic examination showed an ulcerative carcinoma on the greater curvature of the antrum. Histological examination of endoscopic specimens revealed a moderately differentiated adenocarcinoma. Computed tomography (CT) of the chest and abdomen showed no metastasis.

The patient underwent curative gastrectomy for gastric carcinoma with a Billroth I reconstruction. She had no postoperative complications and was discharged from our hospital in March 2005. Approximately 40 per cent of stomach remained and no anastomotic stricture was seen.

Histological examination of the removal specimens showed that the tumor invaded the serosa, and metastases were present in the regional lymph nodes (3/20). She therefore received adjuvant chemotherapy using S-1, which was administered orally twice daily at a dose of 80 mg/m$^2$/day for 28 days followed by 14 days without treatment. This cycle was repeated six times. She had no side effects while on this chemotherapy.

One month after the last chemotherapy cycle, she developed diplopia and horizontal nystagmus. Six weeks after the last cycle, she complained of difficulty walking due to muscle weakness and developed slight confusion. On admission, her symptoms included, diplopia, ballistic movement, anorexia, muscle weakness and disturbance of consciousness. The routine laboratory analysis showed no abnormal findings except for a slightly raised blood glucose concentration. Her blood pressure was 120/64 mmHg. A cardiothoracic ratio was normal on chest X-ray. Although brain CT showed no abnormal changes, magnetic resonance imaging (MRI) of the brain showed a symmetrical high-intensity area in the third ventricle and periaqueductal regions on T2 and Fluid-attenuated inversion recovery (FLAIR)-weighted images (Figure 1, 2A, B). These findings were characteristic of Wernicke's encephalopathy[6,7].

Intravenous thiamine (200 mg/24 hours) and multivitamins were immediately administered. A few hours later her consciousness improved. The next day, the diplopia and ballistic movement diminished, although the difficulty of walking persisted. She began to drink and eat a regular meal within 48 hours of treatment. On the third day she was able to eat an adequate diet and thus the dose of thiamine was reduced to 50 mg daily by mouth. Two months later her nystagmus completely disappeared and she was walking well enough to return to work.

Thiamine tablets were stopped one year after discharge as dietary intake was considered good and she remained asymptomatic. A serum level of thiamine

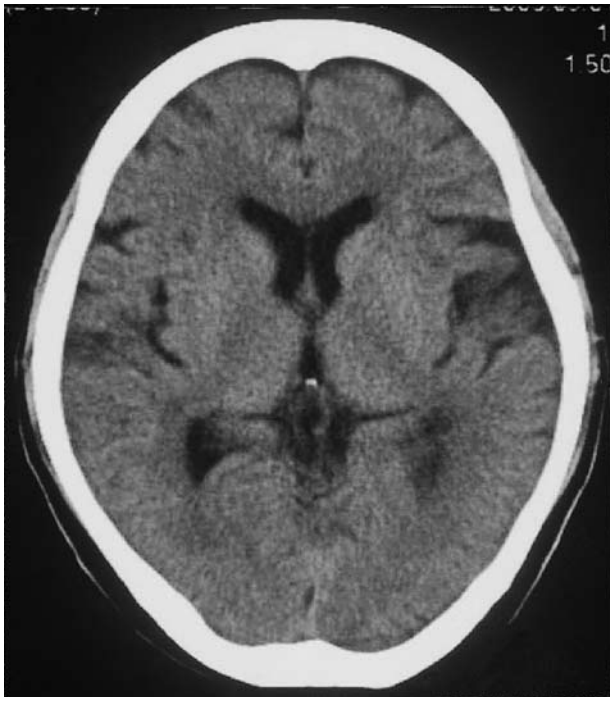

**Figure 1** Brain computed tomography (CT) on admission.
CT showed no abnormal changes.

was 36 ng/ml (normal range : 20～50 ng/ml). However, the thiamine level fell to below normal within one month (17 ng/ml). She had therefore continued on an oral dose of 25mg thiamine daily. At the present time, she has no symptom of Wernicke's encephalopathy.

## DISCUSSION

The amount of thiamine stored in the body is extremely small compared with other vitamins such as vitamins B12 and A. Therefore, thiamine may become depleted within several weeks when dietary intake is insufficient[8]. Failure to correctly diagnose Wernicke's encephalopathy and to promptly administer thiamine can result in coma and death.

The mechanism which gastrectomy causes thiamine deficiency is unclear. Russell et al. have noted that a different mechanism of absorption is used by the body depending on the volume of thiamine ingested[8]. Namely, a low dose of thiamine is absorbed by a carrier-mediated, active transport system, while a high dose is absorbed by a passive mechanism. Thiamine is primarily absorbed through the jejunum[9]. Since thiamine is easily destroyed under alkaline conditions, the high pH in the upper gastrointestinal tract following gastrectomy has been postulated as one of the caus-

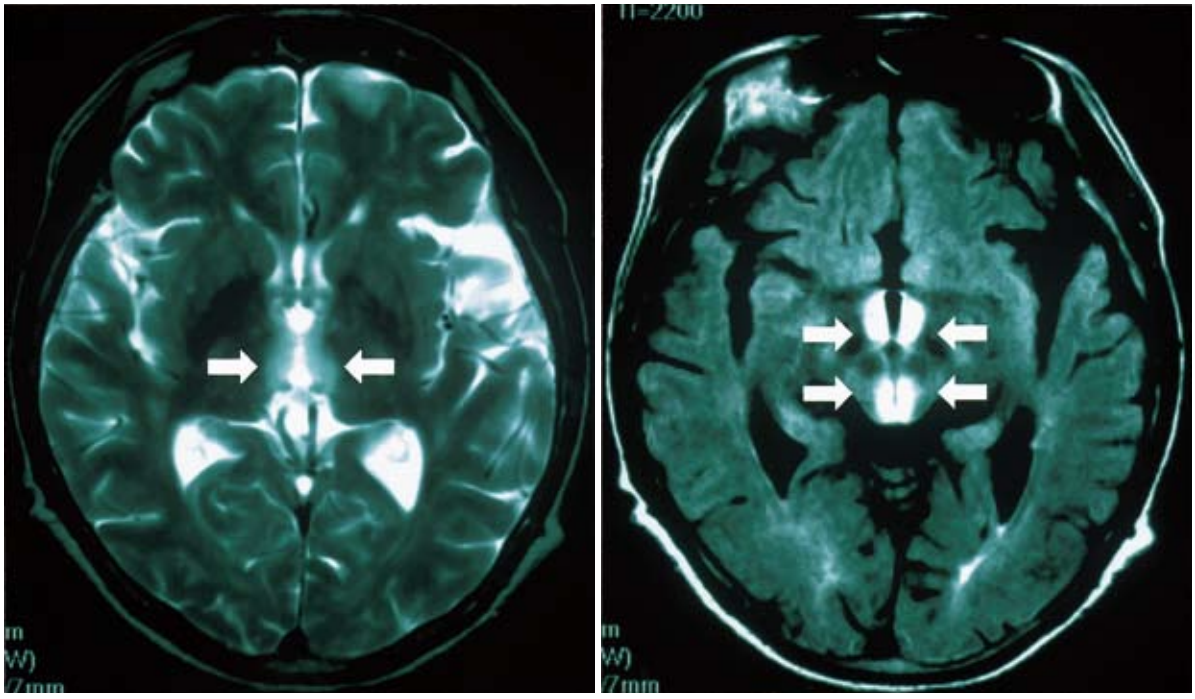

**Figure 2A, B** Brain magnetic resonance imaging (MRI) on admission.
A : T2-weighted MRI shows symmetrical high-intensity areas in the cerebral aqueduct (TR/TE = 4000 ms/100 ms, no. of excitations = 2, section thickness = 7 mm).
B : Fluid-attenuated inversion recovery (FLAIR)-MRI shows symmetrical high-intensity areas in the third ventricle (TR/TE = 6000 ms/120 ms, no. of excitations = 1, section thickness = 7 mm, TI = 2200).

ative factors of postoperative thiamine deficiency [8]. However, Iwase et al. have reported that the method of reconstruction in gastric surgery might not play an important role in postoperative serum thiamine levels [10]

Although the triad of clinical symptoms described by Wernicke (ophthalmoplegia, ataxia, and mental confusion) is diagnostically useful, these symptoms may be singular or multiple, and usually occur suddenly [11]. The clinical diagnosis is often difficult to establish, and CT findings are neither constant nor specific [12,13]. Gallucci et al. reported MRI that is more useful for early diagnosis, because it can clearly demonstrate high-intensity surrounding the 3rd ventricle and aqueduct [7].

In the present case, diplopia and horizontal nystagmus were the initial symptoms, followed by progressive weakness and paralysis in the lower limbs. Several laboratory dates and CT were not helpful in reaching an accurate diagnosis. Eventually, MRI findings prompted the correct diagnosis, and the patient was immediately treated with a large dose of thiamine. Unfortunately, her pretreatment thiamine levels were not obtained prior to treatment ; however, the response to thiamine supplementation suggests that thiamine deficiency induced the symptoms of Wernicke's encephalopathy. Moreover, MRI findings in this case were not different from that caused by 5-FU. In the latter case, MRI usually reveals symmetrical bilateral diffuse high intensity areas in the cerebral white matter on T2-weighted images [14].

S-1, which is becoming more widely used for patients with gastric cancer, may have more worsened the thiamine deficiency caused by distal gastrectomy in our case. S-1, a new oral anticancer drug based on the biological modulation of 5-FU may increase cellular thiamine metabolism, possibly resulting in thiamine deficiency [15~18]. Although the mechanism of 5-FU toxicity is unclear, other studies have shown that 5-FU decreases thiamine by activating thiamine pyrophosphate [19].

Although Wernicke's encephalopathy is relatively rare after gastrectomy for gastric cancer, clinicians must consider the possibility of thiamine deficiency. If the patient shows suspicious symptoms of thiamine de-

ficiency, such as ophthalmoplegia, ataxia, and mental confusion, we should immediately check thiamine levels and the brain MRI of the patient receiving chemotherapy based on S-1 or 5-FU.

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