Diffusion-Weighted MR Imaging in Acute Wernicke's Encephalopathy Associated with Pseudomembranous Colitis: A Case Report and Review of the Literature[1]

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Wernicke's encephalopathy is a common complication of thiamine deficiency among chronic alcoholics. However, there have been few reports about MR imaging findings, including the diffusion-weighted changes of this neurologic disorder, in nonalcoholic patients. We present here a rare case of acute Wernicke's encephalopathy that developed in a patient who received prolonged total parenteral nutrition for his pseudomembranous colitis. The MR imaging, including the diffusion-weighted imaging, was performed at the onset of disease and during follow-up. The diagnosis was made by the characteristic MR imaging findings and it was supported by the clinical features. The initial and follow-up MR imaging findings with diffusion-weighted imaging changes are described and correlated with the clinical status.

Index words : Brain, diseases
Magnetic resonance (MR) imaging
Magnetic resonance (MR) diffusion study

Wernicke's encephalopathy is a potentially fatal neurologic disorder that is caused by a nutritional deficiency of thiamine. This malady is characterized by a classic triad of clinical symptoms that include gait ataxia, ophthalmoplegia and changes in consciousness. The anatomical sites that are most frequently involved in Wernicke's encephalopathy are the mamillary bodies, periaqueductal regions, bilateral medial thalami, third ventricular walls, pons, and medulla (1). Wernicke's encephalopathy has been mainly observed in chronic alcoholics, but it may also be associated with other conditions that prevent adequate amounts of thiamine from being ingested or absorbed. These conditions include protracted parenteral therapy, gastrointestinal disorders, hyperemesis gravidarum and hunger strike (2). To our knowledge, the reports that have described the MR imaging features, including the diffusion-weighted imaging changes, of acute Wernicke's encephalopathy in nonalcoholic patients are very limited. Here, we present a case of acute Wernicke's encephalopathy in a patient who had received total parenteral nutrition for his pseudomembranous colitis. The MR imaging, including the diffusion-weighted imaging, was performed at the onset and during follow-up. The initial and follow-up MR imaging findings with the diffusion-weighted imaging changes are described and correlated with the clinical status.

Case Report

A 69-year-old man was referred to the neurology department because of his altered mental status. The patient had been hospitalized for schizophrenia at another

hospital for two years, during which time he had been treated with risperidone. He had been in his usual state of health until two months earlier, when a sudden onset of repeated diarrhea had developed. He was treated with antibiotics at that time but the diarrhea continued. A colonoscopic examination was performed by a gastroenterologist and a diagnosis of pseudomembranous colitis was made. The patient had been receiving parenteral nutrition through the central venous catheter together with oral metronidazole. After four weeks, the patient was transferred to an intensive care unit in this hospital for acute renal failure. The follow-up colonoscopic examination performed at this hospital revealed improvement of the pseudomembranous colitis. About three days after transferring, the patient suddenly became stuporous.

He had no history of abdominal surgery, hematochezia, melena or any contact with ill persons. He smoked cigarettes, but he did not drink alcohol. On the neurologic examination, he did not open both eyes to painful stimuli, but grimaced symmetrically. There was a limitation on the extraocular muscle movement on the horizontal plane as assessed by the Doll's eye maneuver; however, the pupillary response to the light and the fundoscopic findings were normal. The motor powers were symmetrically reduced to MRC (Medical Research Council) grade 2, but there were no involuntary movements. The deep tendon reflexes were normoactive, and the toe signs showed bilaterally flexing. Any signs of meningeal irritation were absent.

The laboratory findings including the complete blood count, blood chemistry and urine analysis showed no significant abnormality except for mild anemia and slightly elevated liver enzymes. Computed tomography of the brain was performed and it showed no abnormality.

The initial brain MR imaging was performed with a 3-T Achieva system (Philips Medical Systems, Best, The Netherlands), and it showed symmetrical hyperintense abnormalities in the medial thalami, periaqueductal gray matter, tectum of the midbrain and the tegmentum of the lower pons and medulla oblongata on the T2-weighted, FLAIR and diffusion weighted images. The quantitative apparent diffusion coefficient (ADC) maps showed decreased ADC values within the bilateral medial thalami. Although it was difficult to differentiate those affected regions from the surrounding unaffected regions on visual assessment, there were significant differences in measured signal intensities in those two re-

gions on the ADC map ($p < 0.001$). Statistical analysis was performed with a commercially available statistical software program (SigmaStat 3.11, Richmond, California). A paired sample t test was used to determine the statistical significance of the differences between the lesions and the unaffected areas. The mamillary bodies appeared normal in size and they had normal signal intensity. Those affected regions in the brain showed hypointense signals on the T1-weighted images. The periaqueductal regions, tectum of the midbrain and the floor of the fourth ventricle showed slight enhancement on the contrast-enhanced T1-weighted images. On the basis of these MR imaging findings along with his clinical features, a diagnosis of Wernicke's encephalopathy was made.

The patient began receiving treatment with intravenous thiamine as soon as the diagnosis was made and there was steady improvement of his neurologic status. He soon opened his eyes to sound stimuli and recovered from the limitation of eye movements.

About two months after starting intravenous thiamine, he became alert, fully oriented and was able to converse. The follow-up MR imaging was performed; it showed that the previous hyperintensities in the medial thalami, periaqueductal gray matter, tectum of the midbrain and tegmentum of the lower pons and medulla oblongata seen on T2-weighted and diffusion weighted images had disappeared. On the FLAIR images, a weak hyperintense signal was seen in the tectum of the midbrain and the tegmentum of the pons and medulla oblongata. As compared with the initial MR imaging, the third ventricle was slightly enlarged, but the mamillary bodies showed a normal appearance.

Discussion

Wernicke's encephalopathy is a potentially fatal neurologic disorder that is caused by a thiamine nutritional deficiency. In developed countries, Wernicke's encephalopathy has been observed in as many as one fourth of the chronic alcoholics admitted to the general hospitals (3). However, this disorder may also be associated with other conditions that preclude thiamine from being ingested or absorbed in adequate amounts. These clinical conditions include hyperemesis gravidarum, protracted parenteral therapy, gastrointestinal disorders, hunger strike and various debilitating illnesses that impair the appetite, predispose the patient to vomiting or cause protracted diarrhea. In addition, patients with eat-

ing disorders, thyrotoxicosis, severe malnourishment or beriberi are also at high risk for contracting Wernicke's encephalopathy. Most nonalcoholic patients who contract Wernicke's encephalopathy experience only a single and relatively short period of thiamine deficiency (2, 3). Our case was an acute case of Wernicke's encephalopathy that developed in a patient who had been suffering from continuous diarrhea due to pseudomembranous colitis for which he had received prolonged total parenteral nutrition without adequate replacement of thiamine.

Wernicke's encephalopathy is characterized by a classic triad of symptoms that consist of gait ataxia, ophthalmoplegia and changes in consciousness. In many cases, however, the clinical presentation is not complete and only changes in consciousness are present (4). The com-

plete clinical triad of Wernicke's encephalopathy is present in only 16% of cases. Thus, many cases are misdiagnosed during patients' life time, as has been reported by Harper et al (5). Furthermore, when the patient is in a stuporous or comatose state, which makes neurologic examination difficult, the clinical diagnosis of Wernicke's encephalopathy cannot be promptly made. So, in cases that do not present the classical clinical picture, MR imaging is the most important tool for the diagnosis and instituting timely treatment for acute Wernicke's encephalopathy (4). In our case, the initial diagnosis of Wernicke's encephalopathy was made on the basis of the characteristic MR imaging findings. His clinical history of prolonged total parenteral nutrition for treating pseudomembranous colitis and the neurologic findings of ophthalmoplegia with mental distur-
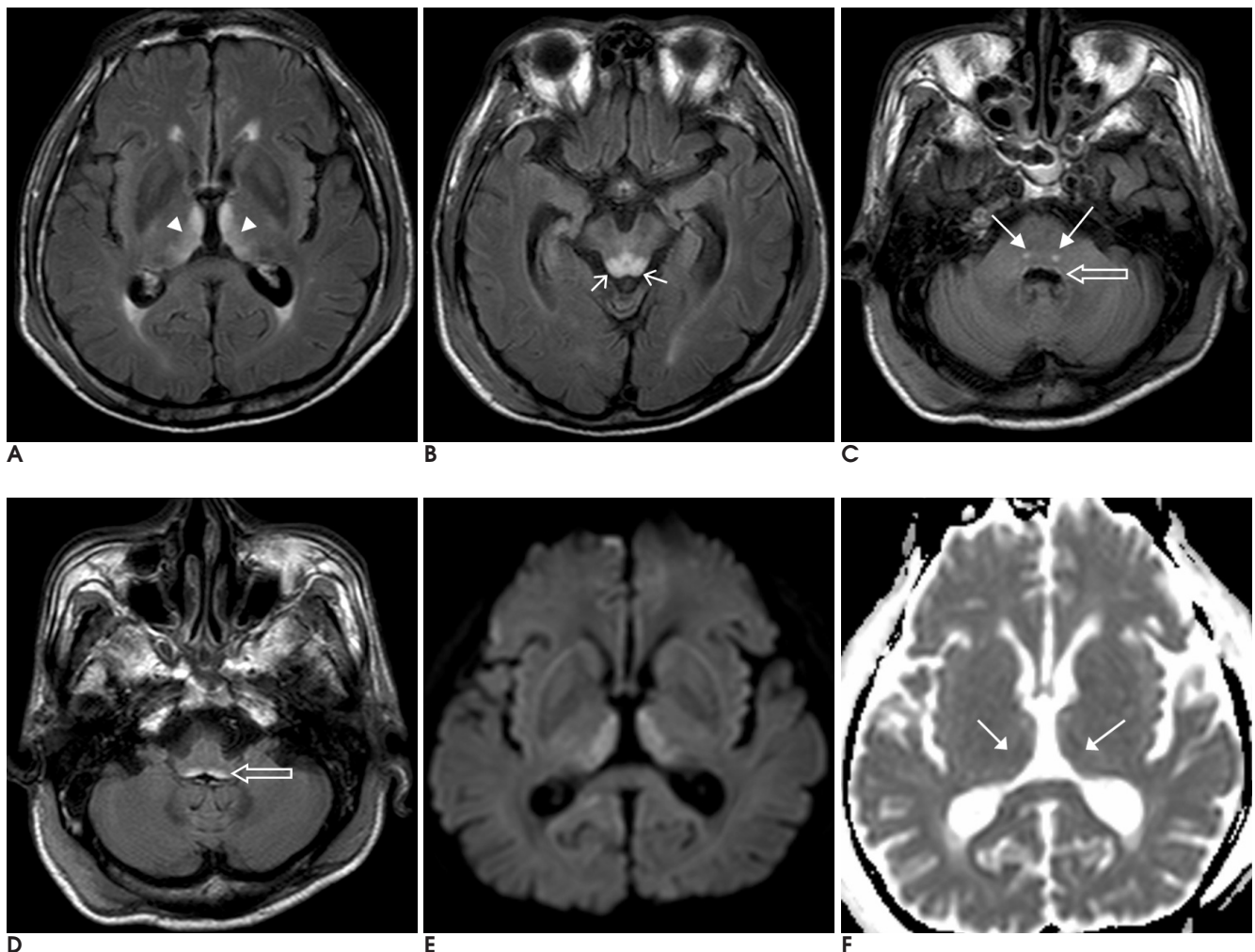

Fig. 1. Acute Wernicke's encephalopathy in a 69-year-old nonalcoholic male patient with pseudomembranous colitis.
A-D. Axial FLAIR images demonstrate abnormal hyperintensities in the bilateral medial thalami (arrowheads), periaqueductal gray matter (small solid arrows), tegmentum of the pons and medulla (open arrows), and the bilateral facial nuclei (solid arrows).
E. Diffusion-weighted image demonstrates symmetrical hyperintense lesions in the bilateral medial thalami.
F. The ADC map demonstrates subtle hypointensities within the bilateral medial thalami.
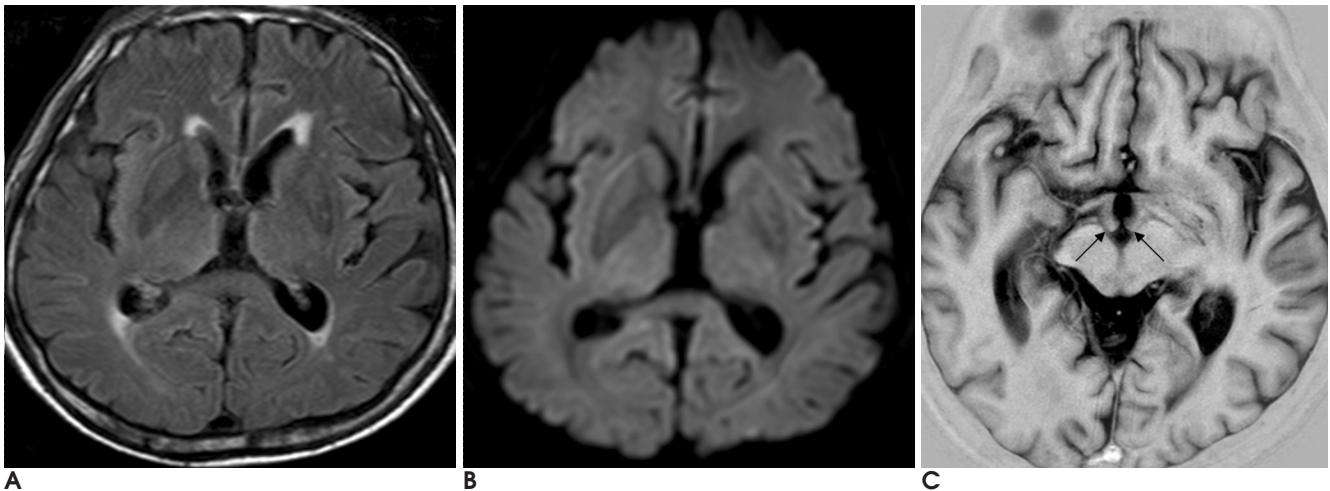
Fig. 2. Follow-up MR imaging performed at approximately two months after starting thiamine treatment. The axial FLAIR image (**A**) and diffusion-weighted images (**B**) demonstrate complete resolution of the previously noted areas of hyperintense signal abnormalities in the bilateral medial thalami. The third ventricle shows slight dilatation compared with the initial MR imaging. The axial T1-weighted inversion recovery image (**C**) demonstrates the normal appearance of the bilateral mamillary bodies (arrows).

bance made the possibility of Wernicke's encephalopathy more likely. The patient's immediate clinical response to the thiamine treatment was consistent with the diagnosis.

MR imaging has been considered the most valuable tool not only for the diagnosis of acute Wernicke's encephalopathy, but also for the evaluation of the pathologic evolution and prognosis of the disorder. Several reports and studies on Wernicke's encephalopathy have described the typical MR imaging features, i.e., symmetric hyperintense signal abnormalities in the periventricular regions of the dorsomedial thalamus, the hypothalamus, mamillary bodies, periaqueductal regions, the floor of the fourth ventricle and the midline cerebellum on the T2-weighted and FLAIR images (4, 6).

The exact pathophysiologic mechanisms that underlie the brain lesions in Wernicke's encephalopathy are not completely understood. Thiamine is a water-soluble essential vitamin obtained from the diet. When thiamine is absorbed from the gut, it is phosphorylated to produce thiamine pyrophosphate, which is a functionally active coenzyme form of the vitamin. As a coenzyme, thiamine has three major functions; these are the oxidative decarboxylation of -keto acids, leading to the synthesis of adenosine triphosphate in the pentose phosphate pathway, and maintaining of neural membrane and normal nerve conduction (3). Thiamine deficiency leads to impaired cerebral energy metabolism, focal lactic acidosis, N-methyl-D-aspartate receptor-mediated excitotoxicity, blood-brain-barrier breakdown and decreased osmotic gradients across cell membranes (7). Donnal et al

(6) have documented that the histopathology at the affected sites ranged from nearly complete tissue necrosis to the presence of reactive glial cells and mild neuronal and myelin destruction. In most of the minimally diseased foci, only proliferation of astrocytes and the prominence of blood vessels were observed, with intact neurons and myelin.

The most frequently involved brain structures in Wernicke's encephalopathy are the periventricular regions, the medial formation of the thalamus, the massa intermedia, the floor of the third ventricle and the mamillary bodies. Victor et al (1) have reported that the most common gross pathologic lesions were mamillary body atrophy, vermian atrophy and cerebellar atrophy in his extensive studies of Wernicke-Korsakoff syndromes. Microscopic lesions were found in all the mamillary bodies and most of the thalami, in which the dorsal medial nuclei were mainly affected. The other brain regions that are affected by Wernicke's encephalopathy include the periaqueductal region at the level of the third cranial nerve nuclei, the reticular formation of the midbrain and the posterior corpora quadrigemina (8).

In our case, most of the involved regions in the brain were the typical ones and they were the bilateral medial thalami, the periaqueductal gray matter, the tectum of the midbrain and the tegmentum of the lower pons and medulla oblongata. These structures were hyperintense on the T2-weighted and FLAIR images. Among those two MR imaging sequences, the FLAIR images demonstrated the affected regions more clearly than did the

T2-weighted images; this is presumably due to MRI's ability to suppress the adjacent cerebrospinal fluid signal intensity that might mask high signal lesions on the T2-weighted images. The affected regions were hypointense on the T1-weighted images. Those affected regions, except the bilateral medial thalami, showed mild enhancement on the contrast-enhanced T1-weighted images. The explanation of this contrast enhancement is probably related to breakdown of the blood-brain barrier, which is one of the relatively early histopathologic changes (7).

There have been a few reports that described atypical MR imaging findings of Wernicke's encephalopathy. Bae et al (9) reported a case with atypical regions in the brain that were involved in Wernicke's encephalopathy, and this was accompanied by bacterial meningitis and brain abscess. MR imaging demonstrated symmetric hyperintense signal abnormalities in the bilateral cerebellar dentate nuclei and red nuclei, in addition to injuries of the tegmentum of the lower pons, bilateral facial nuclei and bilateral vestibular nuclei on the T2-weighted and FLAIR images. In our case, we have found atypical lesions in the bilateral facial nuclei and the tegmentum of the lower pons that were hyperintense on the T2-weighted and FLAIR images.

Diffusion-weighted imaging of our patient with acute Wernicke's encephalopathy demonstrated hyperintense signal abnormalities within the regions corresponding to the areas of increased signal intensities on the T2-weighted and FLAIR images. Among those affected regions, the bilateral medial thalami showed the brightest signal intensity. On the ADC map images, only the bilateral medial thalami showed decreased values of the diffusion coefficients; this is consistent with restricted diffusion and cytotoxic edema. The other affected regions showed an increase in the values of the diffusion coefficients on the ADC maps; this is consistent with the T2-shine-through effect. Halavaara et al (10) have reported that all of their patients with Wernicke's encephalopathy demonstrated increased intensity of the diffusion-weighted imaging signal and increased ADC values in the bilateral medial thalami, except for one patient who demonstrated decreased ADC values in the same regions. They suggested that both cytotoxic and vasogenic edema contributed to the findings observed on diffusion-weighted images and the ADC maps. Although high signal intensity on the diffusion-weighted images and the decreased ADC values in acute Wernicke's encephalopathy are associated with cytotoxic edema, it does not always correspond to irreversible tissue damage (2). Follow-up MR imaging of our case that was obtained two months later showed the absence of the identified signal abnormalities in all the affected areas on the T2-weighted and diffusion-weighted images, although some slight hyperintense signal abnormalities were demonstrated in the periaqueductal region, the floor of the fourth ventricle and the tegmentum of the medulla on the FLAIR images. Several studies have shown that when thiamine is replenished in adequate amounts, the signal abnormalities may normalize within 14 days and this represents reversible cytotoxic edema before the onset of necrosis (2).

Zhong et al (7) reported that the lesions of the bilateral medial thalami were related to the degree of mental disturbance in acute Wernicke's encephalopathy patients. They have found that the patients without coma exhibited only periaqueductal lesions, but all the patients with coma presented with the lesions of the bilateral medial thalami and the head of the caudate nuclei in the acute phase of nonalcoholic Wernicke's encephalopathy. Our case confirmed this relationship between the degree of consciousness disturbance and the damage of the bilateral medial thalami observed on MR imaging in the acute phase of nonalcoholic Wernicke's encephalopathy.

It has been reported that the most common pathologic lesions in Wernicke's encephalopathy are mamillary body atrophy, vermian atrophy and cerebellar atrophy (1). However, a few studies have shown that there is a difference on the MR imaging findings of Wernicke's encephalopathy between alcoholics and the nonalcoholic patients. The difference between the two groups maybe due to the fact that the cerebellar vermis and mamillary bodies are susceptible to thiamine deficiency in alcoholic patients; further, alcoholic patients might have had previous attacks of Wernicke's encephalopathy, and the MR imaging findings in the acute phase were contaminated by previous injury (7). Zhong et al (7) have reported that none of their patients with acute nonalcoholic Wernicke encephalopathy presented with atrophy of the cerebellar vermis and mamillary bodies. Increased signal intensities in the periaqueductal regions, the periventricular regions and the medial thalami on the T2-weighted and FLAIR images were the main findings. Our case did not show atrophy of the cerebellar vermis and mamillary bodies on MR imaging at the onset of disease and during follow-up. We believe that the MR imaging findings of our case clearly demon-

strated the pathologic evolution in the first episode of acute nonalcoholic Wernicke encephalopathy without previous attacks, and it confirmed that the MR imaging findings of nonalcoholic patients are different from those of alcoholics.

In conclusion, we present here a case of acute nonalcoholic Wernicke encephalopathy in which conventional MR imaging and diffusion-weighted imaging were performed at the onset of disease and during follow-up. The signal abnormalities in the brain observed at the initial MR imaging resolved with time and this showed a direct relationship to the clinical symptoms on the follow-up examinations. In addition, diffusion-weighted imaging was advantageous in depicting bilateral medial thalamic lesions and it could be helpful for diagnosing Wernicke's encephalopathy and assessing the patient's prognosis.

References

1. Victor M, Adams RD, Collins GH. The Wernicke-Korsakoff syndrome: a clinical and pathologic study of 245 patients, 82 with post-mortem examination. *Contemp Neurol Ser* 1971;7:1-206

2. Unlu E, Cakir B, Asil T. MRI findings of Wernicke encephalopathy revisited due to hunger strike. *Eur J Radiol* 2006;57:43-53

3. Kane AB, Kumar V. *Environmental and Nutritional Pathology: Nutrition and Disease*. In Kumar V, Abbas AK, Fausto N. *Robbins and Cotran Pathologic Basis of Disease*. 7th ed. Philadelphia: Elsevier Saunders, 2005:456-457

4. Victor M. MR in the diagnosis of Wernicke-Korsakoff syndrome. *AJR Am J Roentgenol* 1990;155:1315-1316

5. Harper CG, Giles M, Finlay-Jones R. Clinical signs in the Wernicke-Korsakoff complex: a retrospective analysis of 131 cases diagnosed at necropsy. *J Neurol Neurosurg Psychiatry* 1986;49:341-345

6. Donnal JF, Heinz ER, Burger PC. MR of reversible thalamic lesions in Wernicke syndrome. *AJNR Am J Neuroradiol* 1990;11:893-894

7. Zhong C, Jin L, Fei G. MR imaging of nonalcoholic wernicke encephalopathy: a follow-up study. *AJNR Am J Neuroradiol* 2005;26:2301-2305

8. Yokote K, Miyagi K, Kuzuhara S, Yamanouchi H, Yamada H. Wernicke encephalopathy: follow-up study by CT and MR. *J Comput Assist Tomogr* 1991;5:835-838

9. Bae SJ, Lee HK, Lee JH, Choi CG, Suh DC. Wernicke's Encephalopathy: atypical manifestation at MR imaging. *AJNR Am J Neuroradiol* 2001;22:1480-1482

10. Halavaara J, Brander A, Lyytinen J, Setala K, Kallela M. Wernicke's encephalopathy: is diffusion-weighted MRI useful- *Neuroradiology* 2003;45:519-523