Clinical Significance of Mammillary Body Enhancement in Wernicke Encephalopathy: Report of 2 Cases and Review of the Literature

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In 2 cases of Wernicke encephalopathy in which the initial symptom was double vision, the only abnormal finding on magnetic resonance (MR) imaging was abnormal enhancement of the mammillary bodies. The mammillary bodies are the region most vulnerable to abnormal enhancement. Because MR imaging with contrast enhancement can detect such abnormal enhancement at an early stage, it should be performed more often in patients with oculomotor disorders to avoid underdiagnosis of Wernicke encephalopathy.

Keywords: contrast enhancement imaging, double vision, mammillary bodies, Wernicke encephalopathy

Introduction

Wernicke encephalopathy (WE) is a neuropsychiatric syndrome resulting from nutritional deficiency of thiamine, or vitamin B1. The classical clinical triad of WE consists of oculomotor disorder, ataxia, and consciousness disturbance. Thiamine deficiency leads to brain lesions in such regions as the medial thalamus, mammillary bodies, periaqueductal region, and floor of the fourth ventricle, all of which depend strongly on glucose metabolism. In all of these regions, magnetic resonance (MR) imaging typically reveals bilaterally symmetrical signal changes. We describe 2 cases of acute WE in which double vision was the initial symptom and the only abnormal finding on MR imaging was enhancement of the mammillary bodies.

Case Reports

Case 1

A 75-year-old woman presented at our hospital with bilateral double vision of several days’ duration. She had undergone radical pancreaticoduodenectomy for treatment of cholangiocarcinoma one and a half years previously. Her vital signs and routine laboratory findings were normal. Neurologic examination at the hospital revealed divergence palsy, mild cognitive impairment, and no other neurologic disturbance, such as muscle weakness, ataxia, or abnormality of the deep tendon reflex. A clinical diagnosis was not made initially, and MR imaging with contrast enhancement was performed to obtain additional information. The only detectable abnormal finding was diffuse symmetric enhancement of the mammillary bodies (Fig. 1A, B). No change in signal intensity was obtained in other vulnerable regions, such as the medial thalami or periaqueductal regions of the midbrain, which are frequently enhanced in WE as seen in T2-weighted (T2WI), fluid-attenuated inversion-recovery (FLAIR), and diffusion-weighted images. Acute WE was proposed, and a decrease in serum thiamine level was confirmed. Supplementation with thiamine rapidly improved the patient’s double vision and mild cognitive functional disorder. One and a half months after the start of therapy, follow-up MR imaging showed near resolution of the abnormal enhancement of the mammillary bodies (Fig. 1C). With continued thiamine administra-
tion, the patient returned to a normal life with no after effects.

Case 2
A 40-year-old man with high levels of alcohol intake and a previous hospital admission for a liver function disorder was transported to our emergency room. He had experienced double vision for the preceding month, subsequently became aware of a disturbance in gait, and gradually noticed loss of strength in both lower limbs. His consciousness was lucid. Physical examination disclosed extorsion restrictions of both eyeballs, lateral gaze nystagmus, gait ataxia, dysesthesia in both lower limbs, muscle weakness, and disappearance of the deep tendon reflex. In consideration of his history of excessive alcohol consumption, gait ataxia, and ophthalmoplegia, acute WE was suspected; accordingly, we tested his serum thiamine level and found it abnormally low. MR imaging with contrast enhancement revealed highly intense gadolinium enhancement only in the mammillary bodies (Fig. 2). No signal changes were detected in other regions. Infusion of thiamine significantly improved the patient’s eye movement the next day, and gait ataxia, dysesthesia, and muscle weakness in the lower limbs improved gradually. Although his ability to move his left eye toward the left remained slightly limited and he continued to experience mild ataxia, he left the hospital with no serious after effects, such as memory deficits.

Review of the literature
We reviewed 106 cases of WE in which MR imaging was performed (Table 1), restricting ourselves to articles concerning 3 or more cases and

Fig. 1. A. Axial fluid-attenuated inversion-recovery (FLAIR) image (2-dimensional [2D], 7-mm slice thickness) shows no change in signal intensity of the mammillary bodies. B. Axial contrast-enhanced image (2D, 5-mm slice thickness) shows diffuse symmetric enhancement of the mammillary bodies. C. Abnormal enhancement of mammillary bodies is almost completely resolved in follow-up magnetic resonance imaging.

Fig. 2. A. No changes in signal intensity of the mammillary bodies were detected in axial fluid-attenuated inversion-recovery (FLAIR) image (2-dimensional [2D], 6-mm slice thickness). Axial (B) and coronal (C) contrast-enhanced image (3-dimensional T1-weighted contrast-enhanced fast field echo [3D T1-CE FFE]) shows symmetric enhancement of the mammillary bodies.
in which MR imaging findings were confirmed. MR imaging with contrast enhancement was performed in 72 of 106 cases, and mammillary body enhancement was detected in 29 of the 72 (40%). In 12 of those 29 cases (41%), plain MR imaging revealed no signal changes in the mammillary bodies.

Including the present case, there have been 5 reports of WE in which abnormal enhancement of the mammillary bodies was the only abnormal finding on MR imaging (Table 2).

### Discussion

We reported 2 cases of WE in which mammillary body enhancement alone was detected on MR imaging and the initial symptom was double vision. In comparison with reported cases (Table 2), our cases are noteworthy in that they were early-stage WE in which severe consciousness disturbance was not observed, and immediate treatment without serious after effects was possible. In consideration of these cases, we propose that in cases in which the initial symptom is an oculomotor disorder such as double vision, the mammillary bodies should be evaluated using MR imaging with contrast enhancement to avoid underdiagnosis of early WE.

Although WE is a simple disease of known etiology, the classic triad is not always present at clinical onset. Clinically, WE has been underdiagnosed, as previous studies have revealed. Harper’s group reported oculomotor disorder to be far more common in their diagnosed group and the absence of eye signs more common in their undiagnosed group. Clearly, clinicians rely heavily on eye signs to diagnose WE. Because oculomotor disorder is both the most noticeable subjective symptom and the most noticeable objective sign, its occasional absence from initial symptoms complicates diagnosis. However, it must be noted that consciousness disturbance can make it difficult for patients to recognize and report subjective oculomotor disorder. Therefore, patients with WE who are capable of reporting their eye signs are likely to be in the early disease stages and have only mild consciousness disturbance, in which case prompt treatment without severe after effects is possible.

Zuccoli and associates reported that abnormal enhancement of brain lesions occurred most frequently in the mammillary bodies, and autopsy analysis has likewise shown this region as the most vulnerable to development of the typical mesencephalic or diencephalic lesions associated with WE. Harper reported the more frequent recognition of microscopic neuropathological findings in mammillary bodies (99%) than in the third ventricle wall (61%), thalamus (61%), or midbrain (50%). The absence of change in signal intensity in the mammillary bodies on plain MR imaging in approximately 41% of cases that demonstrated mammillary body enhancement (Table 1) suggests the

### Table 1. Mammillary body (MB) enhancement in Wernicke encephalopathy: literature review

| Author                  | No. of cases | No. of cases with CE | MB enhancement |
|-------------------------|--------------|----------------------|----------------|
| Mascalchi et al.        | 3            | 2                    | 1              |
| Weidauer et al.         | 12           | 9                    | 4              |
| Fei et al.              | 12           | 3                    | 2              |
| Zuccoli et al.          | 56           | 41                   | 16             |
| Ha et al.               | 23           | 17                   | 6              |
| **Total**               | 106          | 72                   | 29             |

CE, contrast enhancement; *number of cases in which plain magnetic resonance imaging revealed no signal changes in the mammillary bodies

### Table 2. Wernicke encephalopathy in which only mammillary body enhancement was detected on magnetic resonance imaging: literature review

| Author           | Age/Gender | Initial symptom       | Neurological disturbance                        |
|------------------|------------|-----------------------|-------------------------------------------------|
| Shogry et al.    | 59/F       | Dizziness and confusion| Lateral gaze nystagmus, unsteady gait and stance, labile mood, disorientation to time |
| Weidauer et al.  | 37/M       | —                     | Somnolence, disorientation, incomplete gaze palsy, nystagmus |
| Zuccoli et al.   | 45/F       | —                     | Changes in consciousness, ocular abnormalities |
|                  | 62/M       | —                     | Changes in consciousness, ocular abnormalities, ataxia |
|                  | 41/M       | —                     | Changes in consciousness, ocular abnormalities, ataxia |
| Present study    | 75/F       | Double vision         | Divergence palsy, mild cognitive impairment      |
|                  | 40/M       | Double vision         | Restriction of extorsion, lateral gaze nystagmus, ataxia |

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necessity for MR imaging with contrast enhancement to avoid underdiagnosis of acute WE. Abnormalities in the mammillary bodies, which indicate disruption of the blood-brain barrier, are visualized as the first sign of acute WE. Thiamine deficiency impairs ionic gradients across the cell membrane and affects permeability of the blood-brain barrier related to astrocytes before neural necrosis or irreversible structural changes occur.\textsuperscript{10,11} Considering the high frequency of damage of mammillary bodies in acute WE, abnormal enhancement of this region on MR imaging will be an important first sign of WE as it becomes more generally known.

Though the condition of the mammillary bodies should be evaluated via MR imaging to diagnose WE, routine MR imaging does not always reveal extant signal changes in this region, as seen in our cases. Although it is unclear why abnormalities in the mammillary bodies are not detected in plain axial images, the small size of the bodies may make it difficult to detect signal changes. In T\textsubscript{2}WI, in fact, the mammillary bodies are usually lost because their partial volume averages with that of the suprasellar cistern.\textsuperscript{12} Recently, 3-dimensional (3D) FLAIR at 3T has been accepted as a comparatively easy means of evaluating small structures such as the mammillary bodies, and it may be more useful than conventional 2D images for the diagnosis of early WE. In future studies, it will be necessary to compare 3D-FLAIR findings with contrast-enhanced images to determine their relative merit.

When the classical triad of WE is absent or signal changes in typical lesions are not detected on plain MR imaging, WE can easily be underdiagnosed or excluded. Because patients generally complain about oculomotor disorders only when they are not experiencing severe consciousness disturbance, MR imaging with contrast enhancement is recommended in such patients to reveal possible mammillary body enhancement and other findings that are otherwise difficult to detect.

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