Brain SPECT Findings at the Acute Stage of Disease in Patients with Wernicke Encephalopathy

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Abstract

Background: We aimed to objectively examine regional cerebral blood flow at the acute stage of disease in patients with Wernicke encephalopathy.

Methods: We performed single photon emission computed tomography (SPECT) with 99mTc ethylcysteinate dimer in 5 patients with Wernicke encephalopathy, and 15 age- and sex-matched control subjects. SPECT data were analyzed by statistical parametric mapping 8 (SPM8).

Results: SPM8 revealed relative hypoperfusion in the bilateral anterior cingulate gyri and the left inferior frontal gyrus compared to controls.

Conclusion: Our findings suggest that Wernicke encephalopathy affects brain function mainly in the frontal lobe, similar to Korsakoff syndrome.

Keywords: Wernicke encephalopathy; Brain perfusion SPECT; Statistical parametric mapping 8; Limbic system

Introduction

Wernicke's encephalopathy (WE) is an acute neurologic syndrome that results from thiamine deficiency [1]. Chronic alcohol abuse is the most common cause of thiamine deficiency [2]. WE classically presents as a triad of symptoms: altered consciousness, oculomotor abnormalities, and ataxia. Brain imaging techniques, particularly magnetic resonance imaging (MRI) are important and useful in the diagnosis of WE [2-4]. Moreover, functional imaging studies (e.g., positron emission tomography (PET) and single-photon emission computed tomography (SPECT)) provide indirect markers of the function and dysfunction of the neuronal networks involved in WE and Korsakoff syndrome. While many PET and SPECT studies are reported in patients with Korsakoff syndrome [5-10], only one SPECT study has examined brain perfusion in patient with WE [11]. We performed a SPECT study with 99mTc ethylcysteinate dimer (99mTc-ECD SPECT) in patients with WE at the acute stage of disease to evaluate alterations in regional cerebral blood flow (rCBF) using statistical parametric mapping 8 (SPM8) analyses.

Patients and Methods

Subjects

We included five patients with WE (2 men, 3 women; age, 43-67 years; mean age, 56.6) who admitted to the department of neurology, Oita University between 2007 and 2016. Both brain MRI and brain 99mTc-ECD SPECT studies were performed within 30 days of clinical onset of the symptoms. WE was diagnosed based on clinical features, including malnutrition, oculomotor abnormalities, cerebellar dysfunction, an altered mental state, and a good response to thiamine replacement [12]. Information regarding age, sex, drinking history, past surgical history, neurologic symptoms, laboratory tests, and cerebrospinal fluid analysis findings was obtained from the medical records. All patients were treated with 100 mg per day intravenous administration of thiamine for 5-15 days. Fifteen age-matched subjects (mean age 56.9 ± 3.1 years; age range 53-62 years) without neurologic disorders were also included as controls for SPECT image analysis.

Finally, informed consent was received, and all patients or their closest relative agreed to participate in this study.

SPECT image analysis using SPM8

We used the noninvasive Patlak plot method with the fully automated region of interest technique to measure rCBF. Differences in the rCBF between WE patients and the control group were determined by voxel-by-voxel group analysis with SPM8 (Welcome Trust Centre for Neuroimaging, University College, London, UK), running on MATLAB version R2009b (MathWorks, Inc., Natick, MA) according to previous studies [13]. The SPM (t) maps were obtained at a height threshold of P<0.005 (uncorrected) and an extent threshold of 50 voxels. Finally, the Montreal Neurological Institute atlas coordinates were converted to Talairach brain coordinates.

Results

The clinical and demographic characteristics of the patients with WE are provided in Table 1. Four patients were chronic alcoholics and one patient had undergone gastrointestinal surgical procedures. Two of the five patients presented with the classical triad signs of WE, i.e., altered consciousness, oculomotor abnormalities, and ataxia. Two
patients had two signs and one patient had only mild consciousness disturbance. Brain MRI showed high signal intensities on T2- and FLAIR images in the periaqueductal gray matter and bilateral paramedian thalami in patient 1 (Figure 1A and 1B) and in the cerebellum in patient 2 (Figure 1C and 1D). The other three patients had normal MRI findings. SPM8 analysis revealed relatively decreased rCBF in the bilateral anterior cingulate gyri and in the left inferior frontal gyrus in the WE patients compared with the controls (Figure 2 and Table 2).

Table 1: Summary of the clinical and demographic characteristics for patients with Wernicke encephalopathy. M: male; F: female; time interval: time interval of SPECT study from clinical onset.

| Patient | Age/Sex | Time interval | Etiology | Neurological findings | MRI abnormality | Outcome |
|---------|---------|---------------|----------|-----------------------|----------------|---------|
| 1       | 67/F    | 3             | gastrectomy | Consciousness disturbance, ophthamoplesia, nystagmus | +              | Memory loss |
| 2       | 43/M    | 3             | Alcoholic | Consciousness disturbance, ophthamoplesia, nystagmus, ataxia | +              | Ataxia    |
| 3       | 63/M    | 11            | Alcoholic | Mild consciousness disturbance, disorientation | -              | Memory loss, disorientation |
| 4       | 45/M    | 14            | Alcoholic | Consciousness disturbance, nystagmus, ataxia | -              | Ataxia    |
| 5       | 65/F    | 30            | Alcoholic | Consciousness disturbance, ataxia | -              | Confabulation |

Discussion

Brain perfusion images at the acute stage of disease in patients with WE were evaluated using SPM8. Previous SPECT studies of Korsakoff’s syndrome used $^{99m}$Tc-hexamethyl propyleneamine oxime ($^{99m}$Tc-HMPAO) or $^{123}$I-isopropylamphetamine ($^{123}$I-IMP) [5,6]. Our SPECT study used $^{99m}$Tc-ECD, which can evaluate not only brain perfusion, but also the reduction of the enzymatic process due to neuronal dysfunction [13,14]. Patients with WE exhibited significantly decreased rCBF in the bilateral anterior cingulate gyri and in the left inferior frontal gyrus.

There have been several PET or SPECT studies in patients with Korsakoff syndrome. PET studies reported a metabolic reduction in the thalamus, anterior cingulate gyrus, and medial temporal lobe [7-9]. Matsuda et al. [10] reported bilateral decreases in the rCBF or regional cerebral metabolic ratio of oxygen in the frontotemporal areas and left thalamus, suggesting that the cognitive impairments observed in Korsakoff syndrome are due to abnormalities in the frontal-thalamic neural network or Papez circuit. A previous $^{99m}$Tc-HMPAO SPECT study reported decreased rCBF in the frontal lobe [5], whereas an $^{123}$I-IMP SPECT study revealed no hypoperfusion in patients with Korsakoff syndrome [6]. There has been only one case report of WE that showed frontal and frontoparietal hypoperfusion on SPECT [11].

Figure 1: Fluid-attenuated inversion recovery images (axial images) in patients with Wernicke encephalopathy (patients 1 and 2). Patient 1 (A, B) has hyperintense lesions in the periaqueductal gray matter and bilateral paramedian thalami. Patient 2 (C, D) has hyperintense lesions in the cerebellum.

Figure 2: SPM brain map of the group. Group comparison of cerebral blood flow between patients with Wernicke encephalopathy and controls. Wernicke encephalopathy exhibited decreased regional cerebral blood flow in the bilateral anterior cingulate gyri and left inferior frontal gyrus compared with controls.
The anterior cingulate and inferior frontal gyri are considered part of the limbic system, which is associated with vegetative and survival behaviors, emotions, learning, and memory [15].

| Voxel level (Z) | Voxel P (unc) | Talairach coordinates | Region |
|-----------------|--------------|------------------------|--------|
| Wernicke encephalopathy < control | 4.04 | 0.000 | X Y Z | R anterior cingulate |
| 4.03 | 0.000 | -33.66 | -19.04 | -7.68 | L inferior frontal |
| 3.94 | 0.000 | -7.92 | 23.43 | 41.20 | L anterior cingulate |

unc: uncorrected; R: right; L: left; anterior cingulate: anterior cingulate gyrus; inferior frontal: inferior frontal gyrus.

Table 2: Locations and peaks of decreased regional cerebral blood flow in patients with Wernicke encephalopathy compared with controls.

Our SPECT findings at the acute stage of disease in patients with WE revealed decreased rCBF in the bilateral anterior cingulate gyri and in the left inferior frontal gyrus, similar to the PET findings of Korsakoff syndrome. We suggest that the decreased rCBF observed predominantly in the limbic system might be due to secondary changes resulting from degeneration of the frontal-thalamic neural network or Papez circuit.

The present study has several limitations. We diagnosed the patients based solely on clinical findings and did not obtain pathologic confirmation. Due to the small number of patients, the present results should be considered preliminary and should be confirmed by additional studies with more subjects.

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