—Case Reports—

A Case of Reversible Encephalopathy Accompanied by Demyelination Occurring after Ingestion of Sugihiratake Mushrooms

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Abstract

Recently, an outbreak of acute encephalopathy associated with Sugihiratake mushroom ingestion has been reported in northern Japan. Patients with chronic kidney diseases are thought to be at risk for severe encephalopathy following Sugihiratake mushroom ingestion. We report a case of encephalopathy associated with Sugihiratake mushroom ingestion in a patient with diabetic nephropathy. Brain magnetic resonance imaging showed discriminative intensity in the medial temporal lobe, claustrum, and insula cortex bilaterally. Cerebrospinal fluid examination revealed mildly elevated protein and marked elevation of myelin basic protein without pleocytosis. Twenty-five days after admission, these signal-intensity changes had markedly improved, and the patient was discharged without sequelae. Although the exact mechanism of this acute encephalopathy remains undetermined, demyelination is believed to be a possible associated pathological change. In cases of encephalopathy of undetermined cause with distinct magnetic resonance findings, Sugihiratake mushroom intoxication should be considered in areas where ingestion of this mushroom is common.
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Key words: mushroom intoxication, encephalopathy, myelin basic protein, magnetic resonance

Introduction

Several species of mushroom can cause severe intoxication and even fatalities in human beings. Recently, acute encephalopathy related to Sugihiratake mushroom ingestion was reported in northern Japan[1,2]. Sugihiratake is the Japanese name of the fungus *Pleurocybella porrigens*, which is a white, sessile, tongue-shaped mushroom that grows in autumn and is widely distributed in the northern hemisphere, including northern Japan. In the past, this mushroom has been considered an edible species; however, several deaths were reported after ingestion of Sugihiratake mushrooms in 2004. Encephalopathy was also reported to occur

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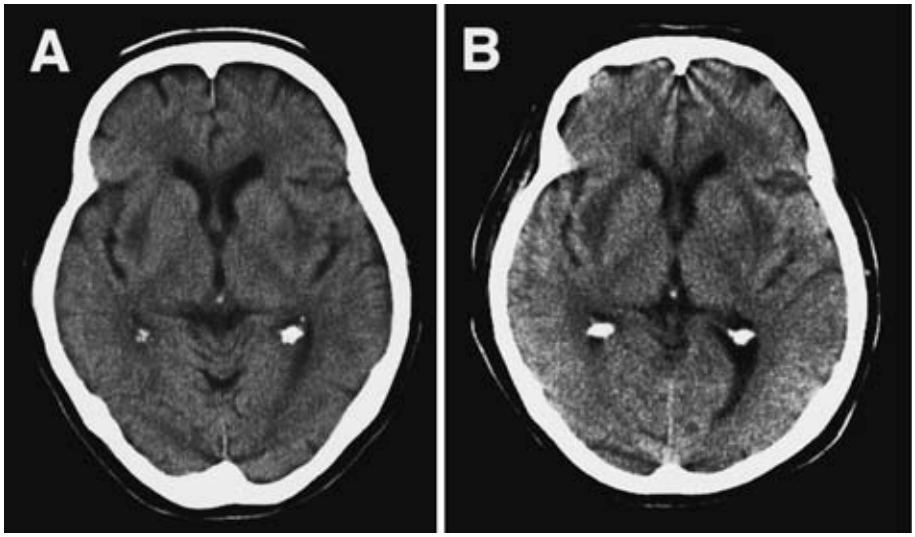

Fig. 1 CT scans obtained on admission and on the following day. Low-density areas were seen bilaterally in the claustrum, insula cortex, and the external portion of the putamen on admission (A). The low-density areas were mildly extended on the following day (B).

exclusively in people who had chronic renal diseases. Here we report acute encephalopathy associated with Sugihiratake mushroom ingestion in a patient with diabetic nephropathy. This case showed distinct magnetic resonance (MR) findings, and cerebrospinal fluid (CSF) examination indicated demyelination. Although the pathophysiology of this type of acute encephalopathy remains unknown, the elevation of myelin basic protein (MBP) levels implicates that demyelination might be a possible associated pathological change.

Case Report

A 71-year-old woman was admitted to our department 2 days after onset of dysarthria and gait disturbance. She had a history of uncontrolled diabetes mellitus and hypertension for more than 10 years. Proteinuria had been present for several years, and serum creatinine levels had gradually increased since the previous year. She habitually ate Sugihiratake mushrooms every autumn since she was 30 years old and had a large quantity of eaten Sugihiratake mushrooms several days before admission. On admission, blood pressure was 175/64 mm Hg, and fever was absent. The patient was somnolent but cooperative and oriented. External ocular movements were normal. She presented dysarthria, mild right hemiparesis including the face without superficial sensory disturbance. Swallowing and protrusion of the tongue were also impaired. Babinski sign was present bilaterally. Computed tomography (CT) showed low-density areas in the bilateral claustrum and insula cortex **(Fig. 1A)**. Fundus examination showed proliferative diabetic retinopathy consistent with the presence of diabetic nephropathy. Admission laboratory data included hemoglobin, 8.7 g/d*l*; white blood cell count, 5,200 per mm^3; C-reactive protein, 0.2 mg/d*l*; VDRL test, negative; blood urea nitrogen, 34.8 mg/d*l*; serum creatinine, 2.0 mg/d*l*; and urine protein, 3+. Possible cerebral infarction was diagnosed, and sodium ozagrel (a thromboxane A2 synthetase inhibitor) and glycerol were administered. The next day, the patient entered a coma and showed tetraplegia. A CT scan of the head the next day showed similar findings **(Fig. 1B)**, and basilar artery occlusive disease was suspected. However, MR on day 4 showed abnormal intensity in the medial temporal lobe, claustrum, and insula cortex bilaterally **(Figs. 2 A～C)**. A CSF examination showed a normal cell count (4 cells/μ*l*), mild elevation of protein (50 mg/d*l*), and normal glucose (93 mg/d*l* for CSF and 141 mg/d*l* for plasma) with normal opening pressure. No bacteria or fungi were identified in the CSF. The IgG index was normal, and an oligoclonal band was

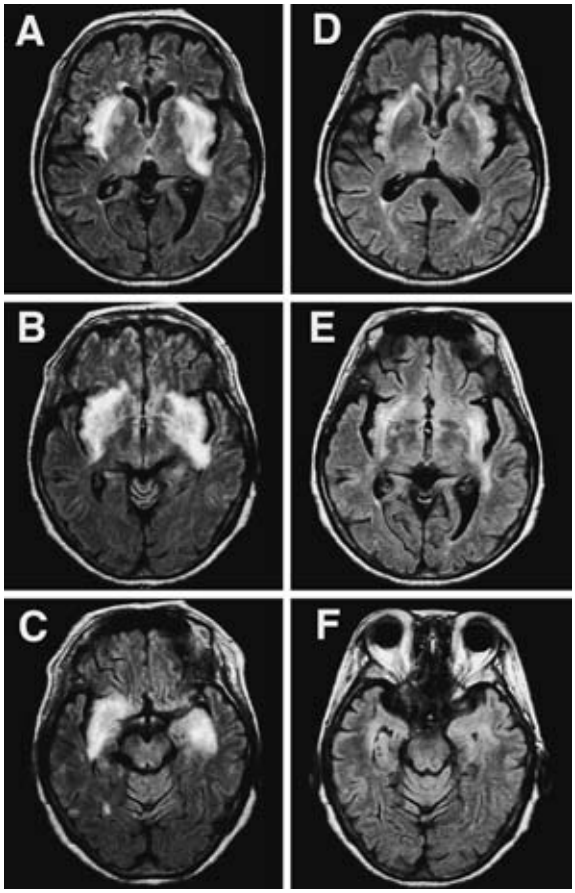

Fig. 2 Fluid-attenuated inversion recovery MR images (TR/TE=10,000 msec/108 msec) obtained 4 days after admission (A, B, and C) and 25 days after admission (D, E, and F). High-intensity signal changes were seen in the medial temporal lobe, claustrum and insula cortex (A, B, and C). Twenty-five days after admission, these signal-intensity changes had markedly improved (D, E, and F).

not detected. The level of MBP was markedly elevated at 672 pg/m*l* (normal range <102 pg/m*l*). There was no significant elevation of antibodies against viruses, including herpes simplex, on sequential CSF studies. Results of extensive laboratory tests, including those for antinuclear antibodies and thyroid function, were within normal range. Although the patient had initially been treated for cerebral infarction, acyclovir was administrated for possible herpetic encephalitis 4 days after admission. Seven days after admission, her level of consciousness had gradually improved. Fifteen days after admission, she could speak, and the tetraparesis had markedly improved. Follow-up MR 25 days after admission revealed significant improvement of the areas of abnormal signal intensity (**Fig. 2D～F**). The level of MBP had recovered to within the normal range 15 days after admission. The patient was discharged without sequelae 44 days after admission. During hospitalization, body temperature was normal, and neck stiffness was not observed.

Discussion

A novel type of encephalopathy associated with Sugihiratake mushroom ingestion was first described by Kato, et al.[2] A review of the history of patients with encephalopathy in northern Japan disclosed that almost all patients who had eaten Sugihiratake had chronic renal disease. The major symptoms are tremor, dysarthria, and weakness of the extremities, followed by severe consciousness disturbance and intractable seizures. Each patient had a history of eating Sugihiratake mushrooms within 2 to 3 weeks before the onset of neurological symptoms.

Kurokawa et al. have reported that T2-weighted MR images in patients with encephalopathy associated with Sugihiratake mushroom ingestion show high-intensity bilateral lesions in the subcortical white matter of the insular cortex, claustrum, external capsule, putamen and globus pallidus[3]. In our case, T2-weighted MR images showed hyperintensity in the bilateral medial temporal lobe, claustrum and insula cortex, similar to that in previous cases. Medial temporal involvement usually suggests herpes simplex encephalitis. Other uncommon entities, such as paraneoplastic limbic encephalopathy, Hurst hemorrhagic leukoencephalitis, gliomatosis cerebri, lupus erythematosus, primary central nervous system lymphoma, and neurosyphilis should also be considered[4]. Our patient did not show fever, neck stiffness, acute inflammatory response, or pleocytosis in the CSF. In addition, there was no significant elevation of antibodies against viruses, including herpes simplex, on sequential CSF studies. These findings argued against aberrant virus infection, including herpes simplex. Moreover, bilateral

symmetrical cortical involvement, reversible monophasic clinical course, and negative antinuclear antibody and VDRL test were not consistent with other known diseases involving the mesiotemporal lobe such as leukoencephalitis, malignant brain tumor, lupus erythematosus, and neurosyphilis.

To our knowledge, this is the first case report showing elevation of MBP in the CSF of a patient with encephalopathy associated with Sugihiratake mushroom ingestion. The MBP was significantly elevated without pleocytosis in the acute phase. On sequential CSF studies, only MBP values changed in parallel with disease activity. The level of MBP in the CSF is a useful clinical marker for assessing various neurological diseases in which myelin is broken down acutely. Increased MBP concentrations have rarely been detected in the CSF of patients with a wide variety of neurological diseases such as myelopathies, encephalopathies, and cerebrovascular diseases[5,6]. Although the pathophysiological mechanism of acute encephalopathy associated with Sugihiratake mushroom ingestion remains unclear, we believe demyelination of the central nervous system could be a pathophysiological mechanism of the disturbance. We suggest that MBP should be evaluated even if routine CSF study shows no abnormalities, and we further propose that MBP might be a useful marker to assess disease activity in this type of encephalopathy.

Gejyo et al. have shown a significant association between Sugihiratake mushroom ingestion and the development of encephalopathy in patients with chronic renal disease, especially those receiving hemodialysis[1]. However, the toxic substance responsible for encephalopathy has not been definitively identified; moreover, they could not explain why only a small percentage of patients receiving hemodialysis showed symptoms or why the disease occurred only in the year 2004. Further studies are needed to answer these questions and clarify the mechanisms of the disease.

In conclusion, to our knowledge this is the first report of elevation of MBP in a patient with possible encephalopathy related to Sugihiratake intoxication. We propose MBP in the CSF should be evaluated in this type of encephalopathy.

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