

Proton MR spectroscopy in the diagnosis of early-stage subacute sclerosing panencephalitis

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ABSTRACT

Subacute sclerosing panencephalitis (SSPE) is a progressive, fatal neurological disorder of childhood and early adolescence. In this report, we present brain magnetic resonance spectroscopy (MRS) and conventional magnetic resonance MR imaging findings of early-stage (stage II) SSPE in an 8-year-old child. MRS demonstrated increased myo-inositol/creatine and choline/creatine ratios, and a decreased N-acetyl aspartate/creatine ratio. Conventional MR imaging demonstrated nonspecific, patchy T2 hyperintensities in the periventricular white matter and a nonspecific focus of T2 hyperintensity in the right frontal subcortical white matter. The MRS findings suggested active inflammation and demyelination as is seen in early-stage SSPE.

Key words: • subacute sclerosing panencephalitis
• magnetic resonance spectroscopy

Subacute sclerosing panencephalitis (SSPE) is a rare, slow virus infection, which is caused by defective measles virus. It is a progressive, fatal neurodegenerative and inflammatory disorder of the central nervous system that usually occurs in childhood and early adolescence (1). SSPE develops after measles infection, following an asymptomatic period of 6 to 8 years. It is diagnosed with clinical findings, electroencephalography (EEG), and cerebrospinal fluid (CSF) features (2). In this report, brain magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) findings of a case with the diagnosis of early stage SSPE are presented.

Case report

An 8-year-old boy was brought to the hospital with complaints of fatigue, tremors of the hands, falling while walking, inability to grasp and hold objects, and speech deterioration, which had started 3-4 days earlier. Before the onset of these complaints, his family had noticed fatigue, slowing of his movements, and behavioral changes, which appeared 20 days earlier. Medical history revealed that he was born by normal vaginal delivery, his mental-motor development was normal, he had no known prior disease, and his vaccines were administered routinely. On his physical examination, he was conscious, oriented, and cooperative, although he gave correct answers to most of the questions, his speech was slow. Bilateral pupillary light reflexes were positive; bilateral pupils were isochoric. Cranial nerves were intact; deep tendon reflexes were normal. Myoclonus presenting as a periodic dropping of the head and loss of tonus was observed. Unwarranted laughing was noted. In EEG examination, periodicity that was thought to be paroxysmal activity, in addition to epileptic activity, were observed. In laboratory examination, blood cell count and blood biochemistry were unremarkable. In cerebrospinal fluid (CSF) examination, protein was 21 mg/dl, glucose was 64 mg/dl, and there was no cell. CSF culture was unremarkable. Raised titers of anti-measles antibodies in the plasma (> 1:180) and CSF (> 1:4) were observed. The patient, with the preliminary diagnosis of SSPE, was referred to our hospital for MR examination and MRS studies. Brain MR imaging and MRS examinations were performed with a 1.5 T system (Siemens Magnetom Symphony, Erlangen, Germany). On brain MR imaging, spin echo T1-weighted (TR/TE: 500/14), turbo spin echo T2-weighted (TR/TE: 4070/73), and turbo FLAIR (TR/TE: 9000/110) sequences on the axial plane were performed, as well as T2-weighted (TR/TE: 3800/95) sequences on the coronal plane. On T2-weighted brain MRI, hyperintense signals whose borders were not clearly distinguished from normal surrounding parenchyma in the periventricular white matter (Figure 1a) and nonspecific focal hyperintensity in the right frontal lobe (Figure 1b) were seen. Proton MRS examination was performed using the chemical shift imag-

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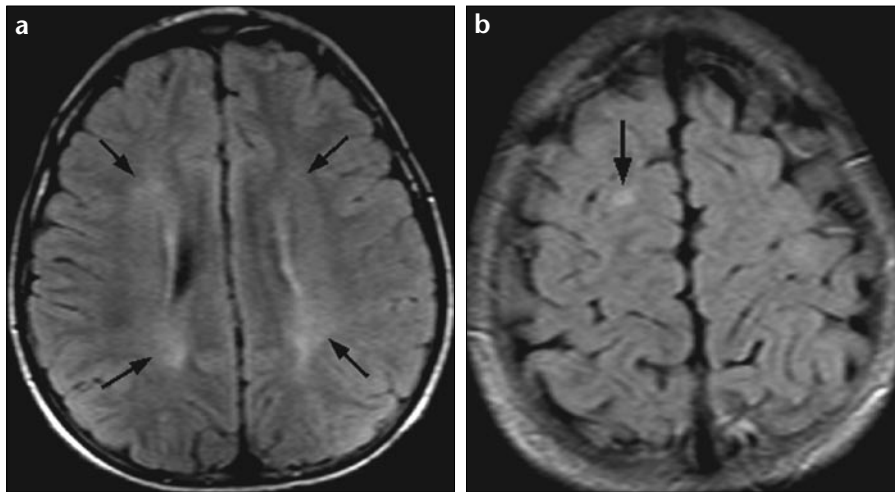


Figure 1. a, b. On transverse turbo FLAIR MR image (a), hyperintense signals whose borders were not clearly distinguished from normal surrounding parenchyma are seen in the periventricular white matter (arrows). On transverse turbo FLAIR MR image (b), non-specific focal hyperintensity is seen in the right frontal lobe (arrow).

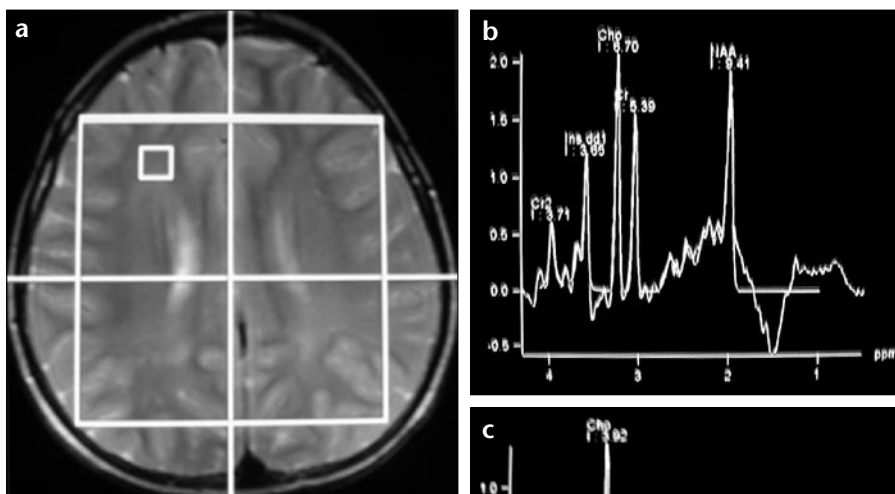


Figure 2. a-c. On transverse T2-weighted image (a), placement of a voxel for multi-voxel MRS imaging is seen. On MRS metabolite spectrum (TE: 30 ms) (b), increase in myo-inositol/creatine and choline/creatine ratios, and a reduction in the N-acetyl aspartate/creatine ratio are seen. On MRS metabolite spectrum (TE: 135 ms) (c), an increase in the choline/creatine ratio and a reduction in the N-acetyl aspartate/creatine ratio are seen. Additionally, prominent lipid peak (at 1.3 ppm) is seen.

ing technique (TR/TE: 1500/30; TR/TE: 1500/135; voxel size: 1 cm³). On MRS examination, an increase in myo-inositol (Ins)/creatine (Cr) and choline (Cho)/Cr ratios, and a reduction in the N-acetyl aspartate (NAA) /Cr ratio were observed (Figure 2). Moreover, on metabolite spectrum with long TE, lipid peak was observed (Figure 2c). MRS findings were consistent with active inflammation-demyelination, which is seen in the early stage of SSPE.

Discussion

Measles is an RNA virus, which belongs to the group of paramyxoviruses (1). SSPE is a slowly progressive and fatal encephalitis form that develops years after measles infection (3). Dawson first described the disease in 1933 (4). The measles virus is thought to reach the brain through infected endothelial cells (5). The measles virus persists silently in the cells of the central nervous system (CNS) and lymphocytes (3). It

is not precisely known how the measles virus remains dormant for so many years and why it becomes active again. It is suggested that an immature immune system fails to destroy the virus completely and the partially degraded virus remains in the CNS. According to another opinion, a simultaneous infection with another virus, such as Epstein-Barr virus, parainfluenza type 1 virus, or toxoplasmosis, causes the measles virus to change. Virus mutations alter the surface antigen of the virus, thereby making it invisible to the immune system. They remain undetected by the host's defense mechanisms for years, and when the immune system becomes suppressed, the virus reproduces and spreads within the CNS (6).

Brain biopsies and postmortem histopathological examinations reveal inflammation of the meninges and brain parenchyma. Neuronal degeneration, gliosis, proliferation of astrocytes, and lymphocytic and plasma cell infiltration in the perivascular and parenchymatous areas were seen. Demyelination was particularly observed in chronic cases (1,7). In SSPE, inflammation of oligodendrocytes results from extensive demyelination (1). In advanced stages, mild to moderate atrophy of the cerebral cortex may be observed. In addition to disorganization of cortical structures, degeneration of neurons may be seen (1). The parieto-occipital region is most frequently involved. The involvement of subcortical and deep white matter becomes most prominent when the disease progresses (8).

SSPE is diagnosed with clinical findings, electroencephalography (EEG), and cerebrospinal fluid (CSF) features.

Clinically, the disease is characterized by personality changes, mental deterioration, myoclonic seizures, and other neurological deficits (7). Jabbour et al. (9) classified clinical SSPE in 4 stages: stage 1 includes personality changes and/or behavioral disturbances; in stage 2, myoclonus, seizures, and severe intellectual disabilities are observed; stage 3 is characterized by rigidity and progressive responsiveness; in stage 4, coma and death are observed. In our case, myoclonus and intellectual disabilities were present, and according to the Jabbour classification, it was classified as stage 2.

The presence of raised titers of anti-measles antibodies in the plasma and CSF is diagnostic for SSPE; levels >1:180

in serum and >1:4 in CSF is diagnostic for SSPE (1). In the presented case, raised levels of anti-measles antibodies in the plasma and CSF enabled us to diagnose the SSPE. Although EEG findings can be normal in early-stage SSPE, the characteristic EEG pattern seen is generalized brief, bilaterally synchronous bursts of spike-wave and/or slow-wave complexes (6).

Computed tomography (CT) findings are generally normal in the early stage of SSPE. As the disease progresses, atrophic changes and hypodensities of white matter are indicative of demyelinating areas (7, 8). MR imaging is a superior method in detecting white matter abnormalities (1, 6). In the early stage, ill-defined hyperintensity areas are observed on T2-weighted images (1). The parietooccipital region is most frequently affected and the involvement is generally asymmetric (10). In advanced stages, signal changes in deep white matter and cerebral atrophy are observed (1). Generally, there is no relation between the clinical stage of disease and MR imaging findings (6, 8).

Although SSPE is a fatal disease, early initiation of treatment slows the progression of the disease and improves the patient's quality of life (11). For these reasons, recognition of and early diagnosis of SSPE are quite important. Nevertheless, the disease is usually diagnosed after permanent brain damage has already taken place. The most important reason for this is that the diagnostic imaging findings appear on CT and MR imaging only after permanent brain damage has occurred. Thus, in the early stages of the disease, additional imaging modalities are needed for aiding the diagnosis.

Brain metabolism can be non-invasively evaluated by MRS. Although MRS is not specific or diagnostic for SSPE, it can show metabolic abnormalities in the white matter in the early stage. Alkan et al. demonstrated increased Ins/Cr and Cho/Cr ratios in stage II SSPE patients, while conventional MR imaging findings were normal. They reported a decreased NAA/Cr ratio in stage III SSPE, while the NAA/Cr ratio was normal in stage II SSPE (10). The increase in the Ins/Cr ratios was explained by glial proliferation, whereas Cho/Cr ratios were explained by demyelination or inflammation. Their explanation for the decreased NAA/Cr ratio in stage III SSPE, while the NAA/Cr ratio was normal in stage II SSPE was that neuronal loss occurs in the late stage. Our case is similar to their study in that we observed an increase in Cho/Cr and Ins/Cr ratios that was especially prominent in short TE (TE: 30). It was thought that the increase in the Cho/Cr ratio was due to active inflammation or demyelination, and the increase in the Ins/Cr ratio was due to glial proliferation. Although our case was clinically stage II SSPE, a decrease in the NAA/Cr ratio was observed, which Alkan et al. noted in stage III SSPE. This finding shows that MRS findings do not correlate with the clinical stage of SSPE, which is similar to the poor correlation between clinical stage and conventional MRI findings that were previously reported (6, 8).

As a result, MRS can provide important information about brain metabolism in clinically early-stage SSPE patients, whereas prominent signal abnormalities are not observed in con-

ventional MR imaging. However, it must be kept in mind that MRS findings do not always correlate with the clinical stage of the patient.

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