An Adult Case of Megalencephalic Leukoencephalopathy with Subcortical Cysts with S93L Mutation in MLC1 Gene: A Case Report and Diffusion MRI

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Dear Sir,

Megalencephalic leukoencephalopathy with subcortical cysts (MLC) is characterized by clinical features including macrocephaly developed within the first year of life, slow deterioration of motor skills due to increasing ataxia and spasticity, mild cognitive impairment and mild clinical course [1–6]. Magnetic resonance imaging (MRI) findings of this disease are well known including diffuse T2 hyperintensity in cerebral white matter and subcortical cysts in the temporal and parietal regions early in its course. However, descriptions of MRI features including diffusion MRI are rare, particularly in adult cases. We report on MRI of an adult MLC case with S93L mutation in the MLC1 gene.

Case Report

A 34-year-old man was admitted to our hospital after a convulsive attack, which had previously occurred only once a few years after his infancy. He was the second child of consanguineous healthy parents. His elder sister was free of neurological problems. Abnormal enlargement of his head developed from the age of 1 year till the age of 3 years. Mild delay in mental and motor development was noted at 2 years of age. A diagnosis of hydrocephalus of unknown cause was made at that time without intensive neuroradiological examination. He had mild mental retardation and spastic gait disturbance; these symptoms remained stable over his teens and were thought to be sequelae of hydrocephalus in his infancy. His medical checks and treatment for epilepsy were discontinued at 20 years. He has worked as a full-time factory worker since the age of 20 years.

Fig. 1. Axial T2-weighted image (a) and coronal FLAIR image (b) show diffuse high signal intensity bilaterally in cerebral white matter including the U fibers. The basal ganglia and the internal capsule are spared. Note a subcortical cyst in the left anterior temporal lobe (arrow).
general subcortical cysts were characterized by high intensity in the anterior temporal and frontal lobes, with diameters ranging from 1 to 2 cm. There was a mild enlargement of the lateral ventricles associated with mild atrophy of the subcortical white matter, most prominently in the parietal lobes and with enlarged cavum septi pellucidi. Diffusion MRI was performed using line scan diffusion MRI [7, 8]. The apparent diffusion coefficient (ADC) value was calculated for abnormal hyperintense white matter and subcortical cysts (Fig. 2). The mean ADC value was $1.69 \pm 0.05 \times 10^{-3}$ mm$^2$/s in affected white matter, much higher than that of normal white matter in age-matched volunteers (mean $0.75 \pm 0.11 \times 10^{-3}$ mm$^2$/s). The mean ADC value of subcortical cysts was $3.02 \pm 0.24 \times 10^{-3}$ mm$^2$/s. Gene analyses revealed that he was homozygous for the S93L mutation of the MLC1 gene.

**Discussion**

Histological examination of MLC reveals cavitating spongiform leukoencephalopathy with vacuoles in the outermost lamellae of myelin sheaths [9]. Subcortical white matter shows intense fibrillary astrogliosis, but myelinated axons are well preserved. Vacularizing leukoencephalopathy is found in several conditions, amongst which are Alexander’s disease, Canavan’s disease, type I glutaric aciduria, L-2-OH-glutaric aciduria, maple-syrup urine disease, Kearns-Sayer disease, merosin-negative congenital muscular dystrophy, and some intoxications. In the acute and subacute stages of vacuolating leukoencephalopathies, diffusion is reported to be restricted, causing low ADC values [10, 11]. Restricted diffusion in vacuolating leukoencephalopathies was shown in Canavan’s disease, Alexander’s disease, maple-syrup urine disease and a case of heroin-induced spongiform leukoencephalopathy. Restricted diffusion pattern in Canavan’s disease accounted for the histopathologic features, including edematous and gelatinous brain tissue associated with diffuse vacuolation [10]. Contrary to other vacuolating leukoencephalopathies with decreased diffusion, all 5 patients (4 children and 1 adult) with MLC reported previously showed increased diffusion and high ADC values [12–14], which is in line with our adult case.

The increased ADC may represent reduced cell density with increased extracellular space, possibly by the coalescence of the small vacuoli, in the white matter. Alexander’s disease and Canavan’s disease are commonly associated with rapid deterioration and severe impairment of neurological function, but variants representing early onset and benign, slowly progressive clinical course protracting into young adulthood are occasionally reported. In addition to specific features of clinical course and conventional MRI findings, the ADC value may be useful to differentiate among vacuolating leukoencephalopathies.

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MLC with S93L Mutation in MLC1 Gene