Reversible Focal Splenium Lesion – MRS Study of a Different Etiology

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Abstract- A 36-year-old man with staphylococcal meningitis had similar symptoms and MRI characteristics as reversible splenium lesion syndrome described in the literature-hyperdensity on DWI and T2WI/FLAIR, hypodensity on ADC, iso-intensity on T1WI, and no contrast enhancement on midline splenium. The splenium lesion on MRI disappeared as the symptoms improved. The etiology of staphylococcal meningitis was different from other reported cases, and the MRS study showed relatively elevated lactate and myo-inositol of splenium as compared to other selective regions in the brain (both white matter and gray matter), which implies increased anaerobic glycolysis and hyperosmolar state on the splenium. The ratios of NAA/Cr, NAA/Cho, and Cho/Cr were abnormal in all selected regions, indicating that the pathologic change involved the whole brain. More series MRS and other advanced exams to correlate intracranial environment (ex. cerebral blood flow, osmolality, inflammatory process, metabolites distribution, and neurotransmitter changes) are needed to confirm the mechanisms of different etiologies with reversible splenium lesion syndrome.

Key Words: Delayed leukoencephalopathy, Heroin, Hypoxia

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INTRODUCTION

Reversible focal splenium lesions, also been termed reversible splenium lesion syndrome (RESLES) recently[(1)], are observed in patients with seizure, antiepileptic drugs withdrawal, metabolic disorders (hypoglycemia or hypernatremia), and viral encephalitis/encephalopathy[(1-6)]. Because of the same characteristics on MRI sequences in differect etiologies–hyperdensity on DWI and T2WI/FLAIR, hypodensity on ADC, iso-intensity on T1WI, and no contrast enhancement on midline splenium[(1-6)]–several hypotheses of mechanism are proposed. One theory is excitotoxic brain edema (intramyelinic edema) attributed to increased extracellular glutamate, which may be induced by increased neuronal activity or metabolic energy failure[(4)]. Some proposed that viral antigens and related antibodies receptors might have specific affinities for splenial axons or surrounded myelin sheath[(6)]. Others postulated alteration of the arginine-vasopression system by starting or withdrawal of pharmaceutical treatment, causing imbalance of brain hydric content[(5)]. Because these hypotheses

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could not explain all the etiologies, the exact mechanism of this phenomenon remains uncertain. We report a patient with a different etiology of RESLES, and performed MRS study to clarify the possible mechanism.

CASE REPORT

W.S, a 36-year-old man, went to a mountain area in Shin-Chiu with his family for 2 days. He felt dizzy and whole head dull pain when returning home. Fever, unsteady gait, slurred speech developed in the following day. A deteriorated consciousness level occurred gradually within 7 days, accompanied with blurred vision, vertigo, photophobia, and dysuria. He was sent to ER, and no skin rash, injected throat, upper respiratory ingrection symptoms, abdomen pain, or stool problems were found by ER doctors. A small scratched skin wound was found on his scalp, but there's no pus and the wound was relatively clean. He did not get insect or animal biting, and had no drug or toxin exposure history. The family who went to the mountain with him were quite well. A neurologist at ER detected bilateral abducens palsy with normal brainstem reflex, negative Babinski sign, and posture/kinetic tremors over bilateral upper limbs. Brain computed tomography (CT) showed no significant abnormalities. Electroencephalography showed diffuse theta to delta waves as background activity, with no sharp waves nor spikes. Cerebrospinal fluid (CSF) studies revealed elevated intracranial pressure (open pressure: 330mm CSF), pleocytosis with lymphocyte predominant (WBC: 44/mm^3, lymphocyte: 38/mm^3), elevated total protein (205mg/dl), decreased CSF glucose and elevated lactate level. Under the suspicion of rhombencephalitis or pathogens that affected specific area of hemisphere, we performed brain magnetic resonance imaging (MRI) on the same day of lumbar puncture procedure. Brain MRI showed ovoid-shaped lesions on the splenium of the corpus callosum, which were hyperintense on FLAIR and DWI, hypointense on ADC, and isointense on T1WI, but were not enhanced by contrast medium (Figs. 1A-E). To exclude neoplasm and infarction, we added MR spectrum (MRS) study, and the MRS

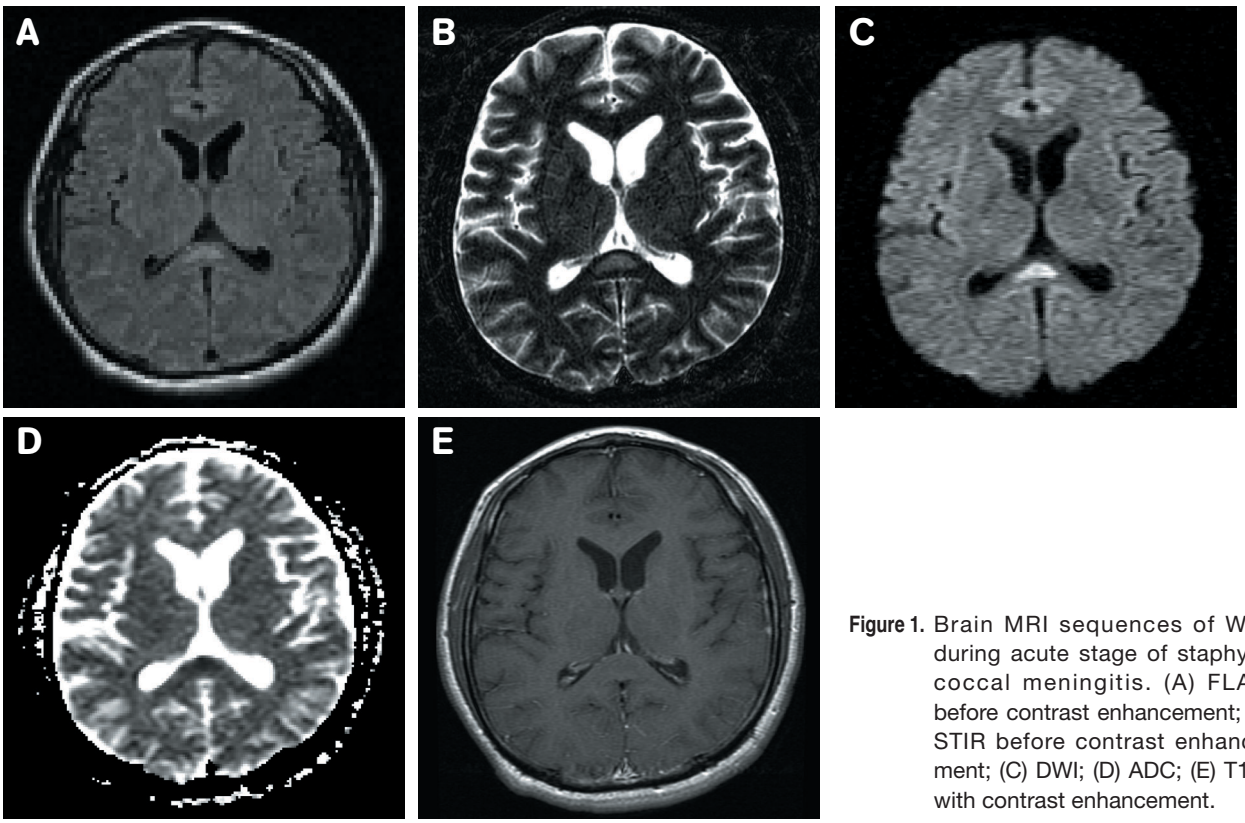

Figure 1. Brain MRI sequences of W.S. during acute stage of staphylococcal meningitis. (A) FLAIR before contrast enhancement; (B) STIR before contrast enhancement; (C) DWI; (D) ADC; (E) T1WI with contrast enhancement.

sequence of splenium lesions demonstrated relatively elevated lactate and myo-inositol levels as compared to other selective regions in the brain (both white matter and gray matter) (Fig. 2), while the ratios of NAA/Cr, NAA/Cho, and Cho/Cr were abnormal in all selected regions. The results of CSF virus detection (including JE virus, CMV, EBV, HIV, HSV, and VDRL) were all normal; TB-PCR and fungus antigen/culture also showed negative findings. Blood and CSF bacterial cultures yielded coagulase negative staphylococcus (CONS). We gave 3rd generation cephalosporin and vancomycin to the patient, and his consciousness level recovered gradually. He was discharged 1 month later, with sequel of occasional forgetfulness and a slightly unsteady gait. He went back to work 2 months later and followed-up brain MRI showed disappearance of the splenium lesions.

DISCUSSION

Staphylococcal meningitis is relatively uncommon in adult, except for immuno-compromised patients, and often accompanied with endocarditis[7,8]. The patient is not immuno-compromised, and there's no evidence of endocarditis. The possible source of infection is a small scratched skin wound on his scalp. We did not get wound culture becaused the skin wound was clean and had no pus. Before referring to our ER, the patient had taken drugs from clinics when fever occurred, and the CSF data suggested partially-treated bacterial meningitis. Blood and CSF cultures confirmed the etiology. We excluded the possibility of acute disseminated encephalomyelitis (ADEM) because there's hypoglycorrhacia in CSF, and no enhancement of the white matter lesions (including splenium) appears on MRI with contrast agent infusion[7,8].

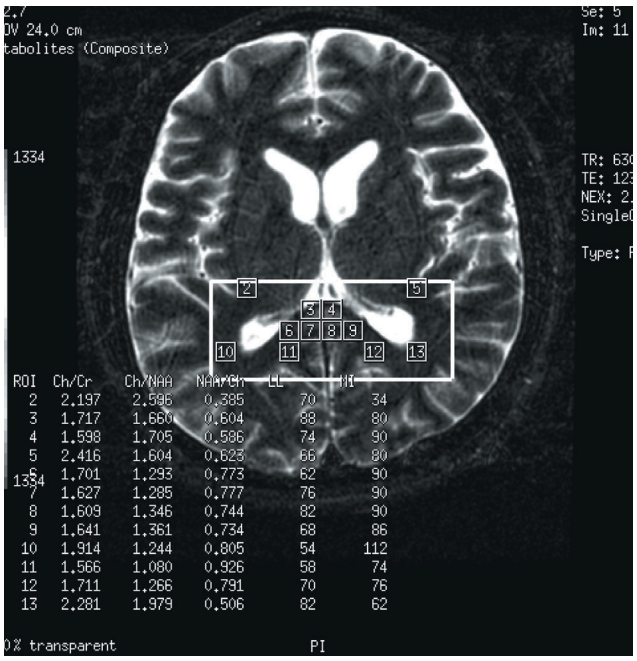

Figure 2. Brain MRI spectrum of W.S. on the splenium lesion and on other areas of white matter during acute stage of staphylococcal meningitis.

The patient's MRI features and clinical symptoms (altered mental state without definite focal neurological signs) were similar to other patients with RESLES described in the literature, but staphylococcal meningitis (or meningoencephalitis?) as the etiology of RESLES has never been reported in previous reports [2,5,6]. The timing of isolated splenium lesion appearing on MRI in our patient is at the "subpial encephalopathy" stage of acute meningeal/ependymal reaction to bacterial infection, which is possibly mediated by cytokines[7]. The normal magnetic resonance angiography and magnetic resonance venography finding excluded arterial infarction or venous thrombosis, and the patient did not have seizures or take any anticonvulsant agents through the course. Disappearance of splenium lesions on MRI correlated with improvement of the patient's clinical condition. The MRS sequence of splenium lesions demonstrated relatively elevated lactate and myo-inositol levels as compared to other selective regions in the brain (both white matter and gray matter) (Fig. 2), which implies increased anaerobic glycolysis and a hyperosmolar state on the splenium. The ratios of NAA/Cr, NAA/Cho, and Cho/Cr were abnormal in all selected regions, indicating that the pathologic changes involved the whole brain.

Although the emergence and remission of the symptoms and signs well correlated with the timing of presence and disappearance of isolated splenium lesions on MRI, the clinical symptoms were not solely attributed to damage of the splenium. The similar concepts were also

mentioned[2,5,6]. We performed the MRS study of RESLES, and found that the reversible splenium lesions with restricted diffusion might reflect alteration of energy/metabolites or homeostatic state in the whole brain (including meningeal and ependymal regions), which could not be detected by current image tools. The relatively increased anaerobic glycolysis and hyperosmolar state on splenium reveals its unique histology and high vulnerability to staphylococcal meningoencephalitis, makes the splenium of corpus callosum a potential marker for certain circumstance changes in the brain. We could not answer whether this phenomenon is attributed to elevated inflammatory chtokines (such as interleukin-6) or specific antigens/sntibodies receptors by the current study.

There are no MRS studies of bacterial CNS infection or other more common etiologies (seizures, AED withdrawal, viral encephalitis, etc.) of RESLES reported in the literature. The MRS study on different etiologies would open a new window regarding the mechanisms and definition of RESLES. More MRS studies and other advanced tests (ex. cerebral blood flow, osmolality, inflammatory process, and metabolites distribution, neurotransmitter changes) to correlate intracranial environment of RESLES are needed. The results of these studies could be applied to managing patients appropriately.

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