A Reversible Stroke-Like Splenial Lesion in Viral Encephalopathy

Weng-Ming Liu[1], Chin-Hsien Lin[1]

Abstract-

Purpose: An ovoid reversible lesion in the central portion of the splenium of the corpus callosum without any accompanying lesions in MRI was uncommon in patients with encephalitis. We aim to report a virus-related encephalitis patient presenting with a reversible isolated ovoid lesion in splenium, mimicking acute infarction.

Case Report: A 32 years old previously healthy man suffered from intermittent fever up to 39˚C accompanied with severe headache, drowsy consciousness, vomiting and diarrhea 2 days before admission. CSF study showed lymphocyte-predominant pleocytosis (lymphocyte/neutrophil 9/0), elevated level of protein (120mg/dL) but normal sugar level (42mg/dL). PCR for HSV-1/2, TB, and influenza antigen were negative. He was diagnosed as possibly virus-related encephalitis and receiving intravenous Acyclovir treatment. Brain MRI showed leptomeningeal enhancement. Notably, one 2.4cm-sized focal lesion with hyperintensity in diffusion weighted image (DWI) and hypointensity in apparent diffusion coefficient (ADC) was noted near the splenium of the corpus callosum, mimicking acute cerebral infarction. Intravenous Acyclovir was kept use and anti-tuberculosis agent (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol) were added. His consciousness gradually recovered 2 weeks after treatment and there was no any neurological sequel left. Follow-up MRI 2 months later was normal without any residual lesions.

Conclusion: Our case confirmed with previous findings that a reversible stroke-like splenial lesion could be seen in virus related encephalopathy and regarded as a good prognosis marker. Transient intramyelinic edema or inflammatory infiltrate is the possible mechanism and further studies enrolling more related cases will be needed to confirm our finding.

Key Words: virus, encephalitis, splenium, corpus callosum, MRI

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INTRODUCTION

Viral infections may lead to central nervous system involvement with the varying clinical spectrums including acute necrotizing encephalopathy and mild encephalitis carrying considerable morbidity and mortality[(1)]. The mechanism by which most types of virus causes encephalopathy remains unclear. Recent evidence shows that proinflammatory cytokines are elevated in the serum and cerebrospinal fluid (CSF) in patients with influenza virus-associated encephalopathy[(2)], suggesting systemic cytokine responses, in addition to

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direct viral invasion, also contributed to the neurological symptoms of viral encephalopathy. Magnetic resonance image (MRI) is a sensitive technique for assisting the diagnosis of encephalitis. A MRI finding of an ovoid reversible lesion in the central portion of the splenium of the corpus callosum (SCC) without any accompanying lesions has been reported in epilepsy patients receiving antiepileptic drugs[3] and some cases with mild encephalitis caused by various agents such as influenza virus and rotavirus[4-6]. These reported cases of encephalitis presenting with the splenial lesion on MRI were clinically mild and had good prognosis. Here, we report a case with virus related encephalitis, which MRI showed a reversible lesion in SCC and discuss the possible mechanism of this reversible splenial lesion.

CASE REPORT

A 32 years old previously healthy man suffered from intermittent fever up to 39˚C accompanied with severe headache, drowsy consciousness, vomiting and diarrhea 2 days before admission. CSF study showed lymphocyte-predominant pleocytosis (lymphocyte/neutrophil : 9/0), elevated level of protein (120 mg/dL) but normal sugar level (42 mg/dL). Polymerase chain reaction for herpes simplex virus type 1 and 2, tuberculosis, and influenza antigen were negative. He was diagnosed as possibly virus-related encephalitis and receiving intravenous Acyclovir treatment. Decreased verbal output, myoclonus and generalized seizure were noted 3 days after admission. Follow-up CSF study showed more elevated level of protein (367 mg/dL) and lymphocytosis (lymphocyte/neutropil: 40/3). Brain MRI showed leptomeningeal enhancement. Notably, one 2.4 cm-sized focal lesion with hyperintensity in diffusion weighted image (DWI) and hypointensity in apparent diffusion coefficient (ADC) was noted near the SCC, mimicking acute cerebral infarction (Figure 1). There were no other intracranial lesions or parenchymal enhancement. His consciousness remained drowsy and had agitation and occasional myoclonus. Intravenous Acyclovir was kept use and anti-tuberculosis agent (Rifampicin, Isoniazid, Pyrazinamide, Ethambutol) were added. His conscious gradually recovered 2 weeks after treatment and there was no any neurological sequel left. Follow-up CSF study 2 weeks later showed decreased total protein (162.5 mg/dL) but still lymphocytic leukocytosis (lymphocyte/neutropil: 99/0). Follow-up MRI 2 months later was normal without any residual lesions (Figure 2).

DISCUSSION

We described a virus-associated encephalitis patient with a reversible isolated lesion in the central splenium of the corpus callosum, mimicking acute infarction on brain MRI. The patient's neurologic symptoms improved two weeks after treatment and no sequel was left. The lesions of the splenium of the corpus callosum on MRI

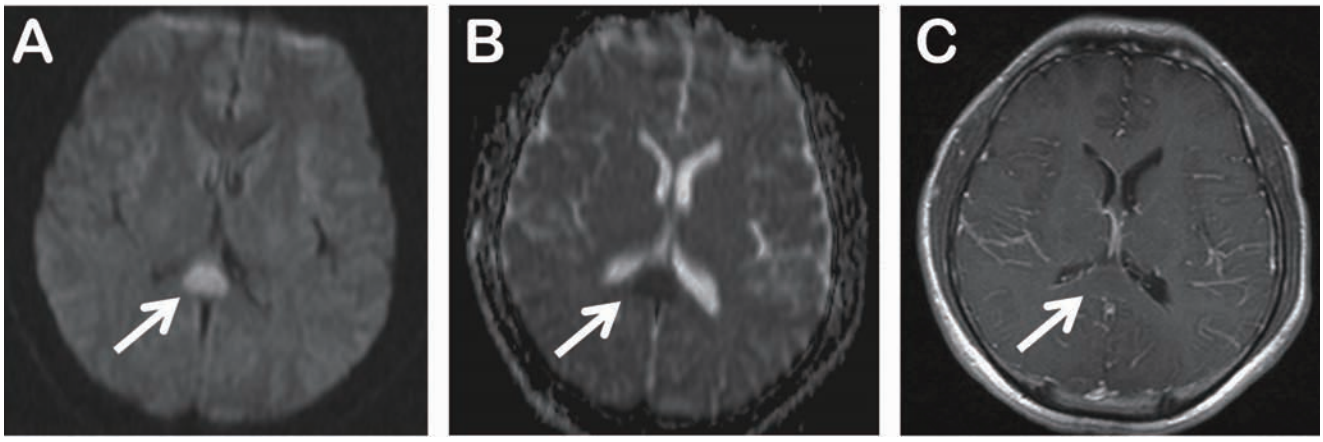

Figure 1. Head MRI images of the patient. Axial view of diffusion weighted image (DWI) (left), apparent diffusion coefficient (ADC) (middle) and T1-weighted images with contrast (right).

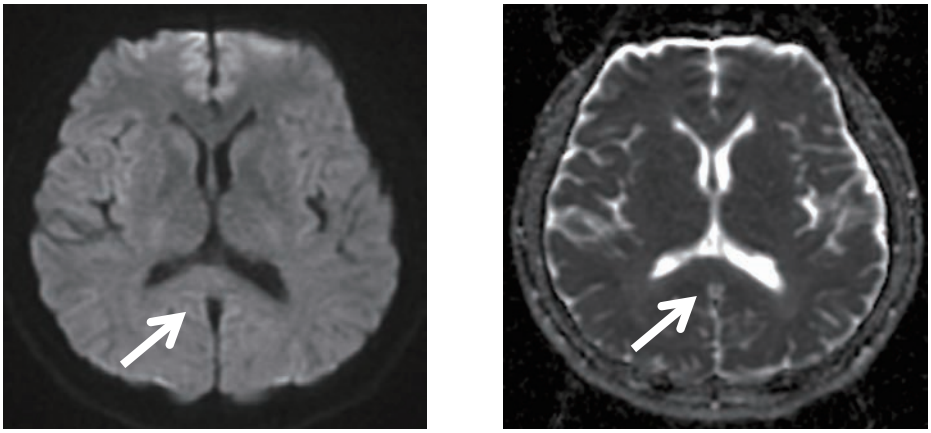

Figure 2. Follow-up head MRI images of the patient. Left image: Axial view of DWI. Right image: ADC image at the same level.

completely disappeared later. Our findings are supportive with previous studies that isolated reversible lesion in splenium of corpus callosum represent a good prognostic marker for benign disease course in patients with encephalitis.

A review of the previous literature have revealed that similar MR findings in the central splenium of the corpus callosum have been reported in some cases of infectious encephalitis with various causative agents, such as influenza virus, rotavirus, and O-157 Escherichia coli, measles virus, and Salmonella enteritidis[4-6]. The clinical manifestations and MR findings were nearly identical to our reported case. All These previously reported cases of encephalitis were clinically mild, and the patients recovered completely. Therefore, although it is unclear about the underlying mechanism of the splenial lesion in these mild encephalitis patients, the completely recovery outcome of these patients suggest MR splenial lesion may be a good prognostic radiologic marker for patients with encephalitis[5].

In patients presenting as encephalitis with focal lesions in MRI, acute disseminated encephalomyelitis (ADEM) should be considered in the differential diagnosis[7]. Since ADEM is a monophasic postinfectious or postvaccinial inflammatory disorder, patients with ADEM presents with alteration of consciousness, focal neurologic signs, and seizure, which develop days to weeks after the onset of presumed viral infections. CSF analysis reveals mild pleocytosis and corticosteroids are useful treatment. However, MRI in ADEM usually shows bilateral and multiple foci in the subcortical white matter with T1 and T2 prolongation[7], which is discordance with the isolated splenial lesion mimicking acute infarction in our case. In addition, the lesions in ADEM often show variable enhancement after contrast treatment, which is contradictory to the findings in our index patient. We therefore speculate our case is clinically and radiologically unlikely to represent a manifestation of ADEM. In addition to ADEM, other differential diagnoses of the central splenial lesion include ischemia, multiple sclerosis, Marchiafava-Bignami disease, metronidazole-induced encephalopathy, CNS lymphoma and extrapontine myelinolysis[8,9]. However, these lesions were excluded clinically and neuro-radiologically in our patient.

The MR imaging of our index patient showed hyperintensity in DWI and hypointensity in ADC on the splenium of the corpus callosum. DWI and ADC are two promising advances in MRI in recent decades, which could image water proton directional “diffusion” as well as “perfusion” processes in a rapid and accurate manner[10]. DWI imaging is shown to effectively allow determination of the presence of anisotropic water diffusion in human cerebral and spinal white matter, which is significantly hampered in cerebral gray matter within the first minutes following ischemic damage. In addition to

DWI, diffusion MRI signatures of brain energetic compromise could also be visualized with ADC imaging, which represents vasogenic edema[11]. In many cases, DWI and ADC images provide complementary data to delineate tissue damaged by ischemia and that abnormal diffusion characteristics can become identifiable within a minute of the complete interruption of blood flow[12]. The occurrence of this stroke-like reversible splenial lesion was first described by Chason et al. in 1996 as a transient post-ictal focal edema denoting transhemispheric propagation of seizure through the corpus callosum[13]. The lesion later has been reported in patients with epilepsy receiving antiepileptic drugs and virus related encephalitis patients[1,3-6]. Notably, in concordance with previous studies, one of the most interesting MRI findings in these encephalitis patients is that the splenial lesion has reversible reduced diffusion ability, which demonstrated as hypodensity in apparent diffusion coefficient (ADC) image. The reversibility within such a short time period suggests that this finding is distinct from energy failure related cytotoxic edema, such as acute infarction. Three possible mechanisms were previously postulated to explain this reversible splenial lesion, including intramyelinic edema, hyponatremia induced interstitial edema and inflammatory infiltrate[5]. Intramyelinic edema may be the cause of the reversible lesion in splenium due to high density of myelin fibers in corpus callosum. However, this speculation was challenged with a previous report that a reversible splenial lesion was observed in a 12-day-old neonate, when the corpus callosum is still incompletely myelinated at this developmental stage[14]. Hyponatremia is another possible contributing factor for the reversible splenial lesion. Hypotonic hyponatremia may result in entry of water into the brain, resulting in partial reversible intramyelinic edema in corpus callosum. Another possible explanation is inflammatory infiltrates of splenium, either directly caused by viral antigens or indirectly antibodies induced by the antigens targeting on splenial axons[14]. Further studies enrolling more patients are needed to clarify the possible mechanism underlying this unique MRI findings in viral encephalitis.

In conclusion, our case demonstrated a reversible stroke-like splenial lesion in a patient with virus-related encephalitis and regarded as a good prognosis marker. Transient intramyelinic edema or inflammatory infiltrate is the possible mechanism and further studies enrolling more related cases will be needed to confirm our finding.

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