CT, MRI and MRS of Epstein-Barr virus infection: case report

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Abstract We report MRI and proton MR spectroscopy (MRS) find-
ings in a 12-month-old girl with Epstein-Barr virus encephalitis. CT and
MRI showed focal lesions in the basal ganglia. MRS of the lesions
showed decreased N-acetyl aspartate and elevation of some amino
acids, indicating an infectious rather than ischemic etiology. This case il-
lustrates the use of MRS to narrow differential diagnosis.

Key words Epstein-Barr virus · Encephalitis · Magnetic resonance
spectroscopy

Introduction

Encephalitis is an uncommon sequel to primary Epstein-Barr virus (EBV) infection, and positive imaging
studies are infrequently reported [1]. We used MR spectroscopy (MRS) to analyze the biochemical char-
acteristics of symmetric basal ganglia lesions in a child with acute neurological deterioration during a sys-
temic illness. The differential diagnosis of the lesions was extensive, but MRS suggested encephalitis, help-
ing to focus the clinical assessment. We know of no prevously published report of MRS in EBV en-
cephalitis.

Case report

A 12-month-old girl presented with a 10 day history of cough and
fever. Chest radiography showed a middle lobe infiltrate. Within
24 h of admission, she had intermittent episodes of opisthotonic
posturing, irritability, and altered responsiveness suggestive of
possible seizure activity. Lumbar puncture revealed no white cells,
4 red cells, protein 10 mg/dl, and glucose 75 mg/dl; culture yielded
no growth. CT showed symmetrically decreased attenuation in the
basal ganglia, without abnormal contrast enhancement. On MRI,
the basal ganglia gave low signal on T1- and high signal on T2-
weighted images (Fig. 1). No other lesions were seen, and there was
no abnormal contrast enhancement.

Single-voxel MRS was performed on an 8 cm3 voxel centered
on the left basal ganglia, at 1.5 T; proton MR spectroscopy was
performed with PROBE-P (Proton brain examination with point-
resolved spectroscopy) acquisition and analysis. Spectra were ac-
quired using short (35 ms) and long (288 ms) echo times with re-
petition time 2000 ms. Spectral analysis showed no evidence of
lactate, a decrease in the ratio of N-acetyl aspartate (NAA) to
creatine (Cr) levels, and elevation of excitatory amino acids, mac-
romolecules and myoinositol (mI) levels (Fig. 2). Composite cho-
line to Cr ratios were normal. Based upon the spectroscopic find-
ings, inflammation/encephalitis was proposed as the explanation
for the basal ganglia lesions, as opposed to ischemia or mitochon-
drial disorders. Serologic studies revealed elevated acute EBV ant-
ibody titers and EBV IgM antinuclear antigen levels. Serum lac-
tate and pyruvate were normal at 1.76 and 0.13 millimol/l, respec-
tively. One month after the onset of symptoms, the patient showed
clinical improvement, but still had choreoathetoid movements of
her limbs and a mild left hemiparesis.
The differential diagnosis of symmetric basal ganglia lesions is extensive. In the acutely ill child, they may be the result of hypoxic or ischemic injury, as in near drowning, hypoglycemia, carbon monoxide poisoning, or perinatal asphyxia. Ingestion of toxins such as methanol, cyanide and ethylene glycol, and certain metabolic derangements, such as Leigh’s disease and other mitochondrial encephalopathies are also considerations. Hepatic encephalopathy, Wilson’s disease, juvenile Huntington’s disease, striatonigral degeneration, and demyelinating diseases such as acute disseminated encephalomyelitis (ADEM) and Lyme encephalitis can also cause symmetric basal ganglia lesions. The basal ganglia are frequently affected in neurofibromatosis type 1, and focal lesions can be seen in dysmyelinating syndromes such as metachromatic leukodystrophy and Canavan’s disease [2].

A member of the herpesvirus family, EBV is recognized as the cause of infectious mononucleosis. Central nervous system (CNS) involvement is uncommon in EBV infection, occurring in less than 10% of cases [3]. Reported CNS manifestations include meningoencephalitis, an altered level of consciousness, Guillain-Barré syndrome, transverse myelitis, cranial nerve palsies, seizures, hallucinations and psychotic features [1, 4, 5]. In their review of 29 cases of EBV encephalitis and encephalomyelitis, Shian and Chi [1] found that all patients presented with an alteration in the level of consciousness, seizures and visual hallucinations being the next most common manifestations [1]. Imaging studies are normal in the majority of children with EBV encephalitis or encephalomyelitis. When abnormalities are detected by neuroimaging, they include foci of T2 prolongation in the deep nuclei (basal ganglia, thalamus) and cerebral cortex [1, 6–8]. EBV has been recognized as a cause of mesenchymalencephalitis [9, 10]. On follow-up MRI focal lesions typically resolve [8]; however, in three children with chronic active EBV infection, Morita et al. [11] found calcification in the basal ganglia, and ADEM has been reported as a sequel to EBV encephalitis [12]. Although it is usually considered a self-limiting disease, Domachowske et al. [5] found residual neurological deficits in 4 of 11 children studied.

The virus has also been associated with postinfectious demyelinating disease [13]. The diversity of lesion location, variable occurrence and duration, and nonspecific clinical presentation combine to make diagnosing EBV encephalitis by neuroimaging alone difficult.

By measuring some of the biochemical characteristics of tissue in vivo, MRS has the potential to increase the specificity of MRI analysis of lesions. The clinical and imaging findings in this case were sufficiently nonspecific to make ischemia, demyelination, inflammation, and direct toxic or metabolic insult all reasonable considerations. Spectroscopy was employed in the hope of narrowing this differential diagnosis. If the lesions were ischemic, as a result of hypoperfusion, hypoxemia, or cellular hypoxia from mitochondrial dysfunction, MRS would be expected to show decreased NAA levels in concert with elevated lactate [14–16]. The low NAA reflects neuronal loss secondary to cell death, while increased lactate reflects conversion to anaerobic glycol-

**Fig. 1** a T2-weighted (2500/100) spin-echo. b FSE FLAIR (10002/142/2200). c contrast-enhanced T1-weighted (500/16) images. The T2-weighted images show symmetric abnormal high signal in the basal ganglia. The contrast-enhanced image shows no abnormal signal or abnormal enhancement.