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Case Report

Transient widespread cortical and splenial lesions in acute encephalitis/encephalopathy associated with primary Epstein–Barr virus infection

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SUMMARY

Infection with Epstein–Barr virus (EBV) is very common and usually occurs in childhood or early adulthood. Encephalitis/encephalopathy is an uncommon but serious neurological complication of EBV. A case of EBV-associated encephalitis/encephalopathy with involvement of reversible widespread cortical and splenial lesions is presented herein. An 8-year-old Chinese girl who presented with fever and headache, followed by seizures and drowsiness, was admitted to the hospital. Magnetic resonance imaging revealed high signal intensities on diffusion-weighted imaging in widespread cortical and splenial lesions. The clinical and laboratory examination results together with the unusual radiology findings suggested acute encephalitis/encephalopathy due to primary EBV infection. After methylprednisolone pulse therapy together with ganciclovir, the patient made a full recovery without any brain lesions. The hallmark clinical–radiological features of this patient included severe encephalitis/encephalopathy at onset, the prompt and complete recovery, and rapidly reversible widespread involvement of the cortex and splenium. Patients with EBV encephalitis/encephalopathy who have multiple lesions, even with the widespread involvement of cortex and splenium of the corpus callosum, may have a favorable outcome with complete disappearance of all brain lesions.

1. Introduction

Epstein–Barr virus (EBV), also called human herpes virus 4, is a member of the herpes virus family. Ninety percent of Chinese people become infected within the first few years of life.[1] Worldwide, EBV infection usually occurs during childhood and does not generally cause clinically symptomatic diseases. However, if primary infection is delayed until adolescence or beyond, it is associated with the clinical syndrome of acute infectious mononucleosis in approximately 25–50% of cases.[2] Moreover, EBV infection is associated with some malignant neoplasms in adults.[3–5] EBV can also result in various neurological complications, especially in immunocompromised patients.

The neurological manifestations of EBV infection were first noted by Epstein and Johansen.[6,7] The occurrence of neurological complications mainly depends on the individual's state of immunocompetence and age, and the forms of complications include encephalitis/encephalopathy, meningitis, cerebellitis, optic neuritis, peripheral neuropathy, cranial nerve palsy, Alice-in-Wonderland syndrome, post-infectious autoimmune disorders including Guillain–Barré syndrome, acute disseminated encephalomyelitis (ADEM), and transverse myelitis.[8] Encephalitis/encephalopathy is an uncommon but serious central nervous system (CNS) complication of EBV,[9] and is sometimes fatal in children.[10]

A case of encephalitis/encephalopathy due to primary EBV infection, in which follow-up magnetic resonance imaging (MRI) showed multiple reversible lesions occurring in the bilateral frontoparietal and occipital lobes, along with a complete clinical recovery within a few weeks, is reported herein. Different magnetic resonance images of viral encephalitis/encephalopathy with transient callosal lesions have been described previously, such as clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS), but to the authors' knowledge no such widespread cortex involvement has been reported as is described in the present case.[10,11]

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2. Case presentation

An 8-year-old Chinese girl was admitted to the hospital from a nearby primary hospital with generalized tonic–clonic seizures and mental deterioration following 1 day of prodromal symptoms consisting of severe headache with vomiting and a high fever (40.0 °C). The patient had previously been healthy and had no past history of infectious mononucleosis. An initial cranial computed tomography scan in the primary hospital was unrevealing. Before admission, she had received acetaminophen as an antipyretic and had been treated with diazepam for epilepsy.

On admission, her Glasgow score (GCS) was 11 (E2, V4, C5) and her vital signs were normal except for a temperature of 38.2 °C. She was drowsy, but did not show any focal neurological signs and was without lymphadenopathy. She had recurrent seizures without regaining consciousness and had to be intubated. Anticonvulsive treatment with midazolam was initiated. Blood laboratory results suggested a marginal leukocytosis (93.4% neutrophil and 3.1% monocytes), but marked atypical lymphocytes were not detected; creatine kinase was elevated (MM 1195 U/l, MB 41 U/l, and BB 56 U/l), but there was no other abnormality. Heterophile antibody testing and EBV capsid antigen antibodies (IgM and IgG) were positive; IgG antibodies against nuclear antigen (EBNA) were negative. Serology for other pathogens including herpes simplex virus (HSV 1 and 2), varicella zoster virus (VZV), *Chlamydia pneumoniae*, *Mycoplasma pneumoniae*, cytomegalovirus (CMV), mumps virus, Japanese encephalitis virus (JEV), measles virus, and ECHO virus showed negative IgM. Cerebrospinal fluid (CSF) analysis showed an abnormal cell count (125×10^6 white cells/l, 75% lymphocytes), protein of 11 mg/dl (reference range 0–40 mg/dl for children aged 6 months to 10 years), glucose of 4.38 mmol/l (corresponding to blood sugar of 6.12 mmol/l), and chloride of 128.3 mmol/l (reference range 120–132 mmol/l), with a pressure of 190 mmH_2O. CSF viral capsid antigen IgM was positive. A quantitative real-time EBV PCR assay for CSF was positive and quite high (26 400 copies/ml).[12] Results of the CSF analysis showed the absence of nucleic acid of HSV (1 and 2), CMV, VZV, and *M. pneumoniae*. No conclusive evidence of autoimmune rheumatic disorders was found.

Table 1
MRI sequence parameters

	T1WI	T2WI	DWI	FLAIR
TR, ms	2205	3540	6500	8000
TE, ms	22.5	98	90	169
FOV, mm	240	240	240	240
Matrix	512 × 512	512 × 512	256 × 256	256 × 256
Thickness, mm	7.5	7.5	7.5	7.5
b, s/mm^2	-	-	1000	-

MRI, magnetic resonance imaging; WI, weighted imaging; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; TR, repetition time; TE, echo time; FOV, field of view.

A brain MRI scan was initially performed with a 3.0-T unit (Signa HDxt; GE Health) including T1-weighted (T1W), T2-weighted (T2W), fluid-attenuated inversion recovery (FLAIR), and diffusion-weighted imaging (DWI) sequences. The parameters of the MRI protocol are reported in Table 1. The images showed widespread DWI signal intensity hyperintensities in different cortical areas, especially the bilateral and symmetrical parieto-occipital areas, which were most marked in the splenium of the corpus callosum, with involvement of the white matter of the left posterior horn. The T1W, T2W, and FLAIR sequences did not show obvious signal abnormalities except slight T1W hypointensity and T2W hyperintensity in the splenium (Figure 1). Therefore, the MRI findings suggested a cytotoxic edema.

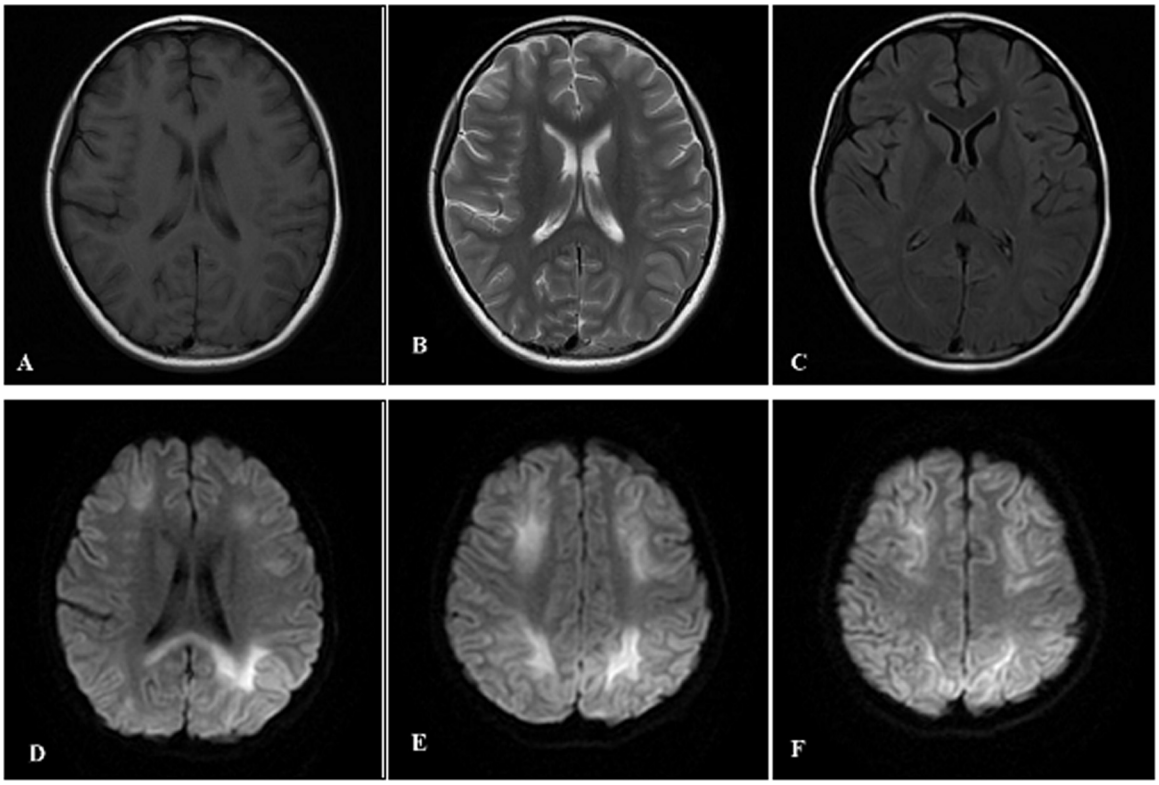

Figure 1. T1W (A), T2W (B), and FLAIR (C) sequences of the initial 3.0-T MRI did not show obvious signal abnormalities, except slight T1W hypointensity (A) and T2W hyperintensity (B) in the splenium. However, widespread DWI signal intensity hyperintensities were shown in different cortical areas, especially bilateral and symmetrical parieto-occipital areas (E and F), and were most marked in the splenium of the corpus callosum (D), with involvement of the white matter of the left posterior horn.