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CASE REPORT

Progressive Multifocal Leukoencephalopathy in a Child as First Manifestation of Congenital Human Immunodeficiency Virus Infection

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ABSTRACT

This report is of a 13-year-old girl who presented with progressive multifocal leukoencephalopathy as the first manifestation of congenital human immunodeficiency virus infection. Progressive multifocal leukoencephalopathy is a severe demyelinating disease of the central nervous system caused by JC papovavirus infection. The prognosis is poor, with a fatal outcome within 1 year for 90% of patients.

Key Words: *Adolescent; Demyelinating diseases; HIV*

中文摘要

首發症狀為進行性多灶性腦白質病的先天性人免疫缺陷病毒(HIV)感染兒童

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本文報導一例感染先天性人免疫缺陷病毒(HIV)，首發症狀為進行性多灶性腦白質病的13歲女童情況。進行性多灶性腦白質病是由一種JC病毒(乳頭狀瘤多瘤空泡形病毒)感染引起的中樞神經系統嚴重脫髓鞘病變。該病預後很差，1年內死亡率達90%。

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system caused by JC papovavirus infection. In PML, the oligodendroglial cells are affected, resulting in multiple foci of demyelination.[1,2] PML typically occurs in immunocompromised individuals, such as patients with congenital human immunodeficiency virus (HIV) infection or other conditions associated with impaired T-cell function.[2,3] Clinically, PML presents as relentlessly progressive focal central nervous system dysfunction, such as hemiparesis, aphasia, cortical blindness, or altered mental states.[1] The death rate from PML is considerably increased if it is associated with acquired immunodeficiency syndrome (AIDS).[4] The mortality rate is 90% within 1 year of diagnosis.[3]

The clinical diagnosis of PML is made either by the detection of JC virus DNA in cerebrospinal fluid[5,6] or isolation of the JC virus in brain biopsy. This report is

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of a girl who presented with PML as the first manifestation of congenital HIV infection.

CASE REPORT

A 13-year-old girl presented in 2009 with impaired right hand movements, which gradually progressed to right hemiparesis. She also had increasing difficulty with facial expression for 1 month. At examination, she had right facial paralysis, right hemiparesis, and right hemianopia, without evidence of encephalopathy. The patient had good past health except for a history of herpes zoster at the age of 6 years, from which she had an uneventful recovery with conservative treatment.

Urgent computed tomography (CT) of the brain showed a few hypodensities in the white matter of the left occipitoparietal region, left basal ganglia, and left thalamus. Magnetic resonance imaging (MRI) confirmed the presence of multifocal demyelination in these regions (Figure 1). There was no significant mass effect or contrast enhancement. On diffusion-weighted imaging (DWI), a few areas of restricted diffusion were present in the left thalamus, basal ganglia, and left corona radiata (Figure 2), which were consistent with cytotoxic oedema. The patient also underwent brain biopsy, which showed features compatible with PML. There was no evidence of malignancy or lymphoma. Cerebrospinal fluid (CSF) was also positive for polyomavirus DNA. Subsequent laboratory investigations showed that the patient was positive for antibody to HIV, and she was diagnosed with HIV infection. Her CD4 count was 36 L/μL (reference range, 600-1100 L/μL). On further questioning, her mother disclosed that she had been infected with HIV since 1992, and received regular highly active antiretroviral therapy (HAART). This patient was also given HAART, which resulted in a marked decrease in viral load and improvement in CD4 count.

Initially, she showed some improvement in cognitive function with better clarity of speech. However, 4 months later, she had further deterioration in her general condition, with worsening of the right-sided weakness and increasing left-sided weakness, such that she lost her ability to walk. Follow-up MRI of the brain showed progression of the white matter changes in the entire left hemisphere, associated with atrophy (Figure 3). There were also new areas of demyelination in the contralateral right cerebrum and brainstem (Figure 4). Previous areas of restricted diffusion were resolved and became T1-hypointense, indicating tissue necrosis after the initial cytotoxic oedema.

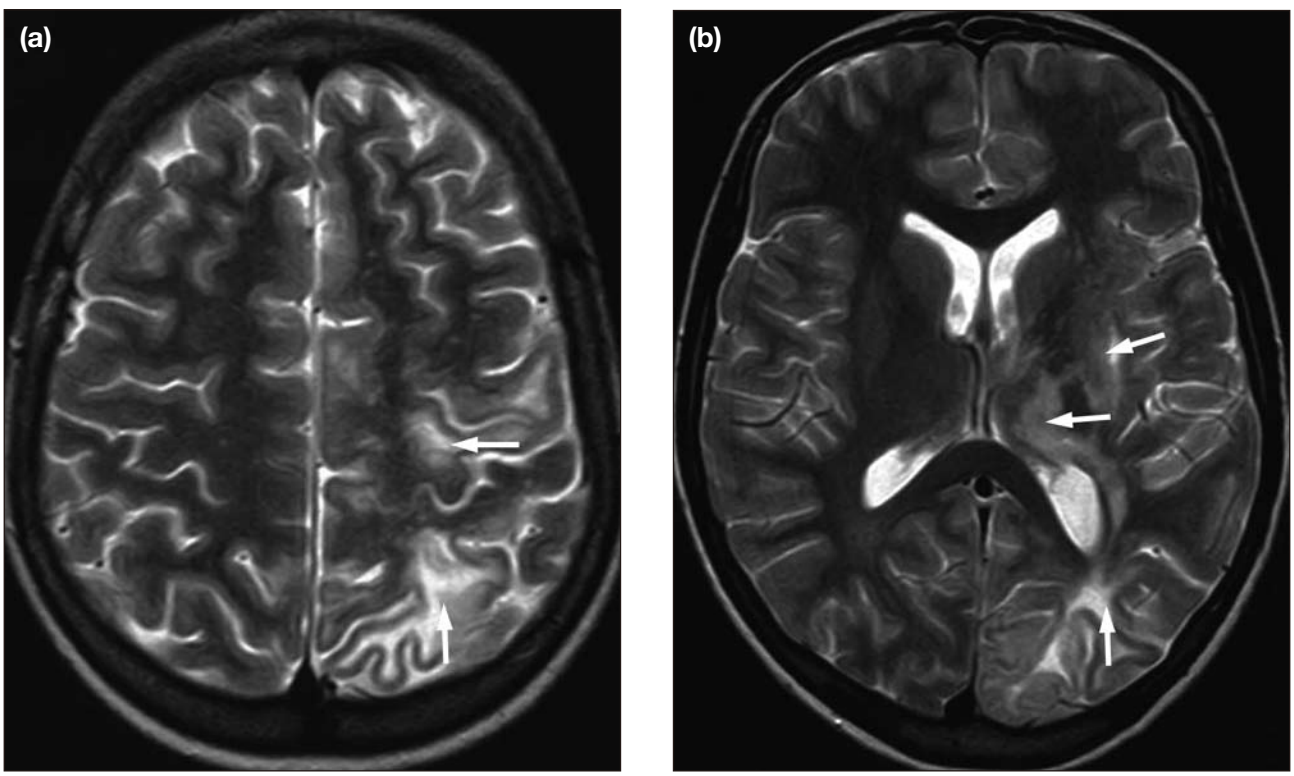

Figure 1. Axial T2-weighted magnetic resonance images of the brain at presentation showing focal T2-hyperintense areas in (a) the left parieto-occipital and precentral white matter (arrows); and (b) the left thalamus and basal ganglia (arrows).

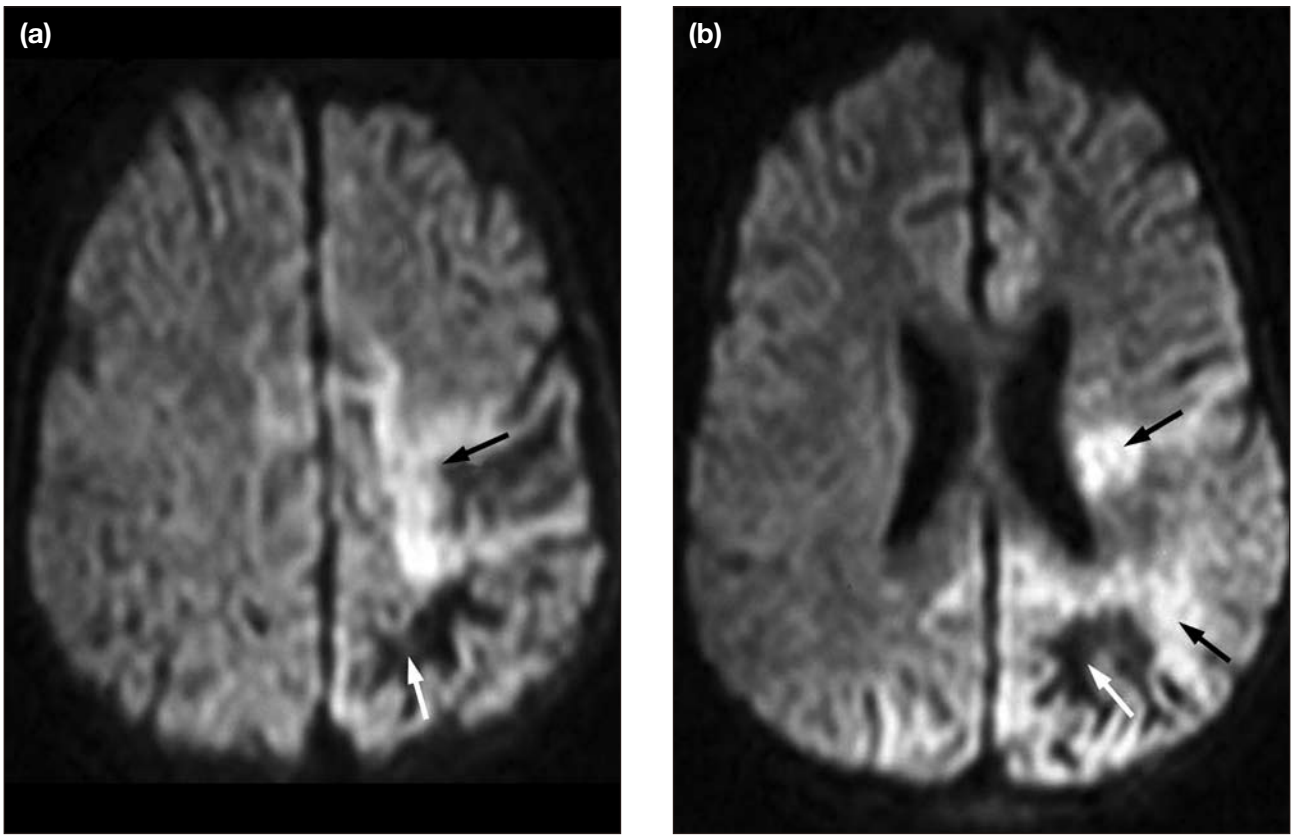

Figure 2. Diffusion-weighted magnetic resonance images of the brain at presentation showing focal bright areas of reduced diffusion in (a) the left centrum semiovale and (b) the corona radiata white matter indicating cytotoxic edema (black arrows). The white matter at the left parietooccipital region (white arrow) does not have restricted diffusion and corresponds to areas of tissue necrosis.

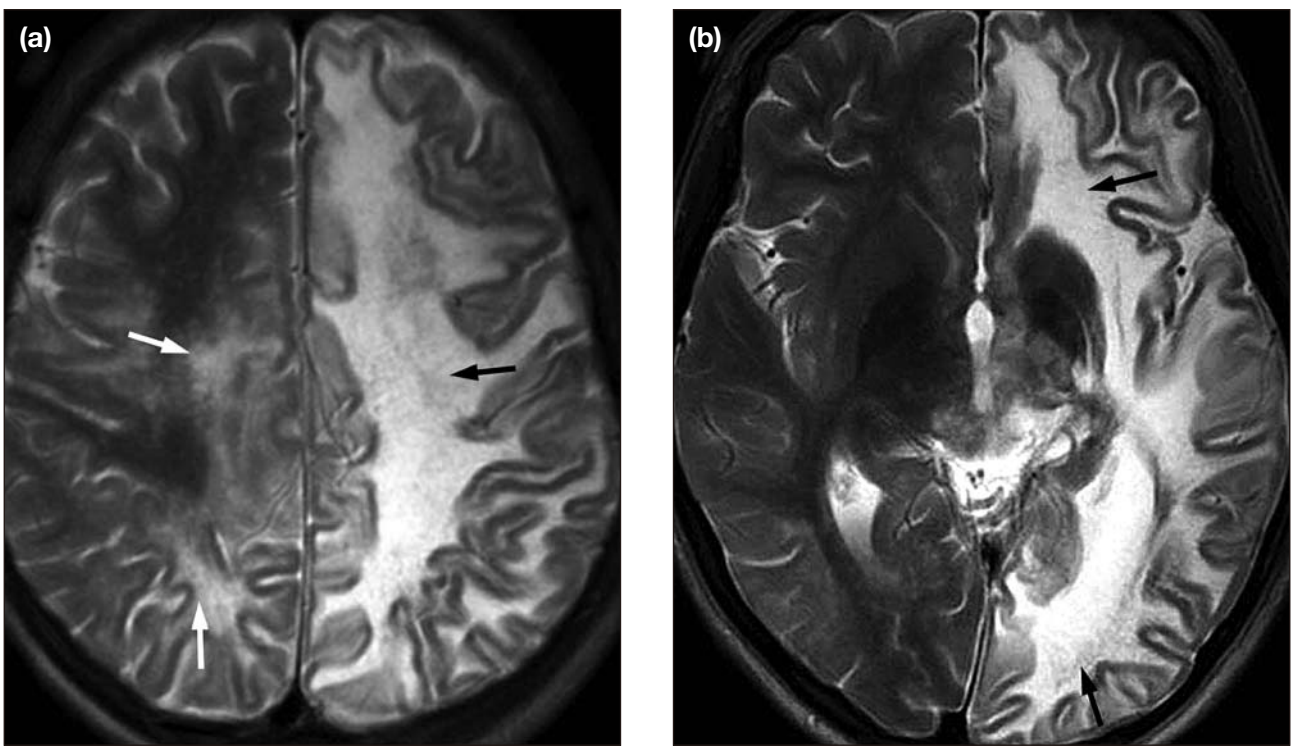

Figure 3. Follow-up T2-weighted axial magnetic resonance images at 4 months showing progression of demyelination within the entire left hemisphere (black arrows). (a) There are a few new areas of demyelination in the right centrum semiovale and parietooccipital regions (white arrow); and (b) the left cerebral sulcal spaces are widened suggestive of generalized left cerebral atrophy.

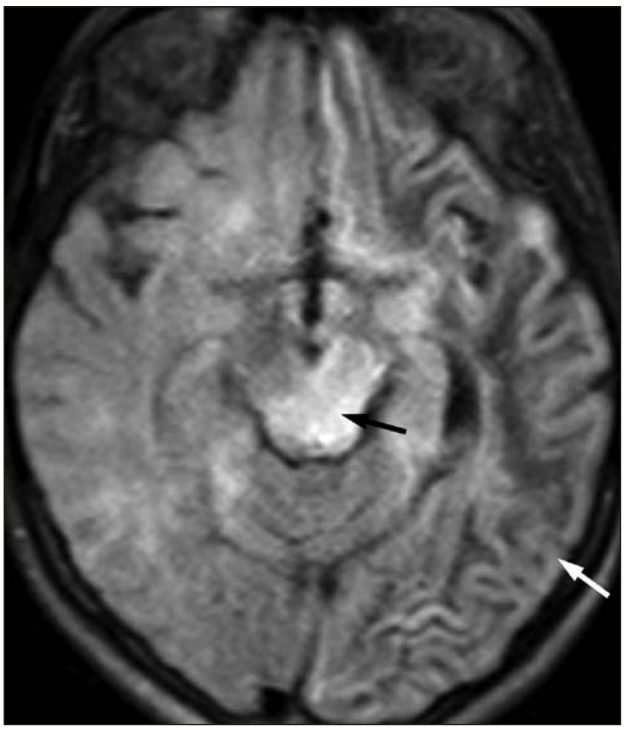

Figure 4. Follow-up axial fluid attenuated inversion recovery magnetic resonance image at 4 months showing T2 hyperintensity of the brainstem (black arrow) indicating severe demyelination. There was left cerebral atrophy (white arrow).

DISCUSSION

MRI is the preferred imaging method for diagnosis of PML. Typically, PML appears as widespread asymmetric lesions in the white matter. These lesions are T2-hyperintense with little or no mass effect, and usually do not enhance after contrast administration. The absence of mass effect and enhancement is distinct in PML and distinguish PML from other conditions in immunocompromised patients, such as lymphoma and toxoplasmosis.[7,8] In this patient, the diagnosis was apparent as the lesions did not show a mass effect or contrast enhancement.

Several MRI findings have been reported to correlate with outcome and survival. In a large multicenter study by Post et al, mass effect was found to be the sole imaging feature associated with mortality in patients with PML.[1] However, mass effect associated with PML is uncommon and therefore is not a useful prognostic sign in the clinical setting. DWI is a recent MRI technique that has proven its value in evaluating brain tissue injury by quantifying isotropic water diffusion rates. DWI enables differentiation of vasogenic from cytotoxic oedema.[9] By measuring the entire diffusion tensor, the degree of anisotropic diffusion within the brain can be quantified.

DWI is therefore useful for evaluating PML, in which the microstructural integrity and myelination of the brain is affected. Two recent studies have shown evidence of altered isotropic and anisotropic diffusion in normal-looking white matter in adult patients with HIV infection.[10,11] Fractional anisotropy measurements have been found to be more prognostic than apparent diffusion coefficient values in predicting the prevalence of dementia in patients with PML.[11] Two other studies have also shown that DWI could be used to monitor the degree of demyelination and tissue destruction in adult patients with PML.[2,12]

In conclusion, although the definitive diagnosis of PML is based on brain biopsy or CSF culture, MRI is helpful clinically in several ways. First, MRI is useful for initial detection and delineation of cerebral lesions when neurological symptoms first appear. Second, MRI can help to differentiate PML from other neurological manifestations of HIV such as lymphoma and toxoplasmosis. Third, MRI is useful for monitoring the progression of the disease. Conventional MRI sequence scan accurately depicts acute from chronic PML lesions, while DWI can provide objective measurement with prognostic significance.

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