Diffusion Tensor Images and Magnetic Resonance Spectroscopy in Primary Central Nervous System T-cell lymphoma: A Case Report

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Abstract-

Purpose: Primary central nervous system lymphoma (PCNSL) is rare and usually B cell in origin. T-cell lymphoma constitutes only 1.8% to 4.6% of the PCNSL, and may present as solitary or multiple homogeneous enhanced lesions. There have been few reports showing unusual leukoencephalopathy in PCNSL, which may be confused with other white matter diseases including multiple sclerosis and acute disseminated encephalomyelitis.

Case Report: We reported a patient with T-cell PCNSL who presented a progressive dull response and extra-pyramidal symptoms. Brain magnetic resonance imaging showed multiple focal leukoencephalopathy. Diffusion weighted imaging demonstrated hyper-intensity lesions and apparent diffusion coefficient images showed hypo-intensity lesions. Diffuse tensor images showed decreased fractional anisotropy. Pathology examination finally confirmed T-cell lymphoma.

Conclusion: Although recent development of neuro-imaging studies, the diagnosis of PCNSL still await further pathological confinnation in some occasions.

Key Words: primary central nervous system lymphoma, leukoencephalopathy, T-cell lymphoma, neuroimaging, magnetic resonance imaging, diffuse tensor image.

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INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is a rare tumor in the nervous system without any evidence of systemic lymphoma. The prevalence of PCNSL increased recently because of increased incidence of patients with acquired immunodeficiency syndrome or an immune compromised state[1]. The PCNSL is usually B cell in origin, while T-cell lymphoma is very rare, constituting of 1.8% to 4.6% of PCNSL in western countries[2-4]. Most PCNSL may present as solitary or multiple homogeneous enhanced lesions[5,6]. However, diagnostic challenge may occur if the lesions present in unusual leukoencephalopathy[7-9]. Recently,

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new development of neuro-imaging studies shows a great potential to improve accuracy of diagnosis. In this study, we describe a patient with T cell PCNSL (T-PCNSL) who presented as unusual leukoencephalopathy. The differential diagnosis among various neurological diseases is discussed.

CASE REPORT

A 57-year-old man had hypertension, diabetes mellitus, and atrial fibrillation for 10 years with regular medication control. He developed subtle behavior changes including impairment in concentration while performing exercises and poor sleep for 3 months. Intermittent numbness, clumsiness with slow motion, and rigidity were noted in the right hand 1 month later, followed by left hand clumsiness, and festinating gait with a flexion posture. He became irritable, restless, and agitated, and had inappropriate behavior in his friends' wedding. He also had a slow response and poor memory; sometimes he forgot to turn off the light and tap water. Slurred speech and difficulty dressing were also observed in recent one month.

During physical examinalions, there were no palpable lymph nodes. Neurological examinations showed clear consciousness but a slow response, poor memory, slurred speech and dysphasia were noted. There were neither pyramidal signs, nor sensory abnormalities. However, he had obvious extra-pyramidal symptoms including rigidity in bilateml hands, bradykinesia, masked face and a festinating gait. Palmo-mental reflex was noted in right side. Left arm focal seizure developed after admission.

Laboratory findings disclosed normal hemograms, electrolytes, and liver, renal, and thyroid functions. Tumor markers including carcinoembryonic antigen, prostate specific antigen and α-fetoprotein were normal. Autoimmune factors such as anti-nuclear antibody, C3, C4 and rheumatoid factor were also in the normal ranges. Antibody for human immunodeficiency virus was negative. Cerebrospinal fluid study revealed white cell count 2/μL, red cell count 0/μL, sugar 70 mg/dL

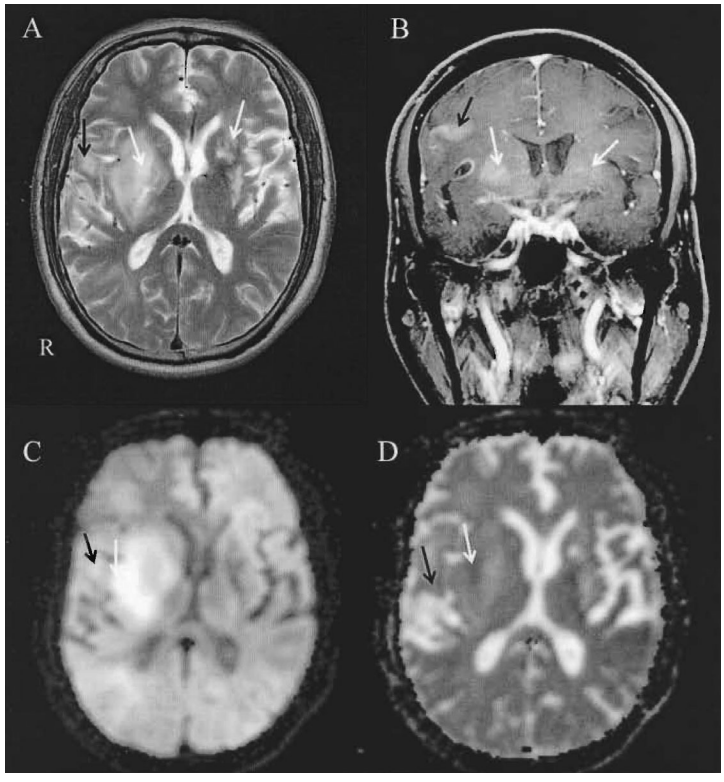

Figure 1. A: Brain T2-weighted MR images showed hyperintense lesions in the bilateral basal ganglia especially right side (white arrows) and right parietal subcortical white matter (black arrows).
B: After contrast medium administration, homogeneous enhancement was noted in bilateral basal ganglia especially right side (white arrows) and right parietal region (black arrows).
C: Diffusion weighted imaging (DWI) demonstrated hyperintensity lesions in the right parietal subcortical white matter (black arrows) and right basal ganglion (white arrows).
D: Apparent diffusion coefficient (ADC) image (equal to mean diffusivity) showed hypointensity of the right basal ganglion (white arrows) and right parietal area (black arrows).

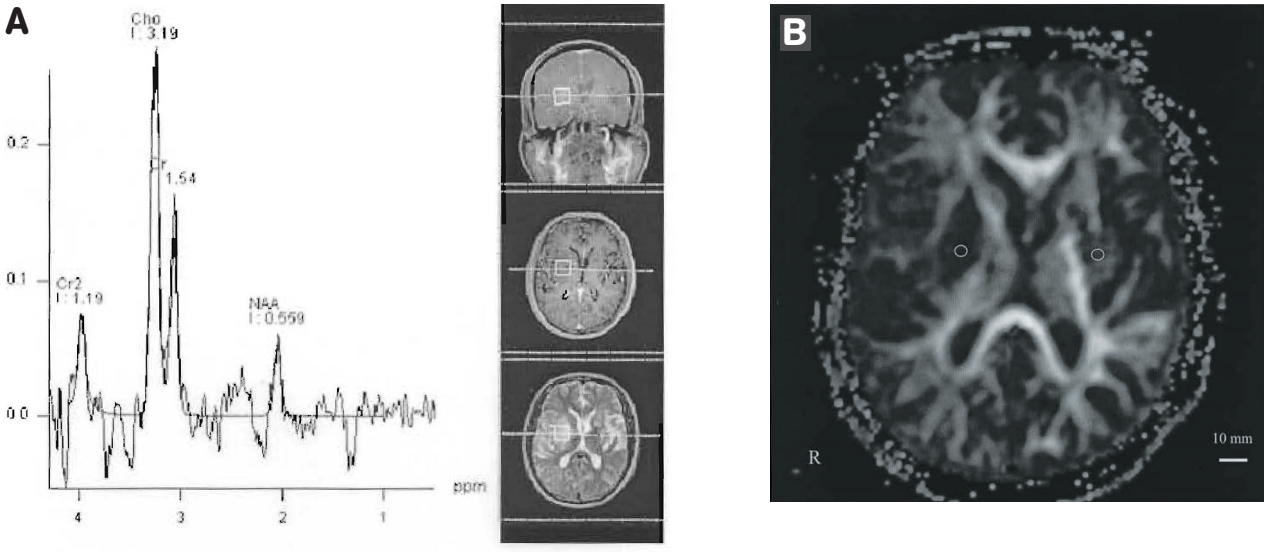

Figure 2. A: Brain magnetic resonance spectroscopy showed an elevation of choline peak and depressed N-acetylaspartate. B: Brain diffusion tensor image (DTI) showed decreased fractional anisotropy (FA) of the bilateral basal ganglia. (right FA= 0.083 v.s. left FA= 0.111) (circle area).

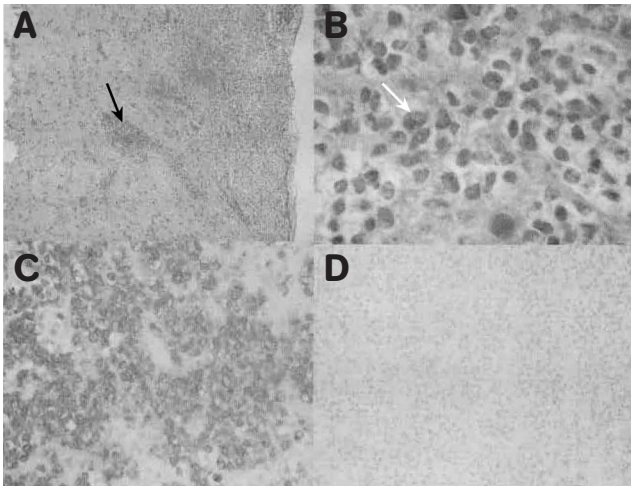

Figure 3. Brain biopsy from the right basal ganglion (A) showing perivascular cuffing with tumor cell infiltration (black arrows) (H&E stain, 20X), (B) lymphoid cells with hyperchromatic nuclei and perinuclear halo (white arrows) (H&E stain, 400X). Immunohistochemical stain showing (C) CD3 positive staining (200X) and (D) CD20 negative staining. (200X)

(blood sugar 108 mg/dL), protein 39.2 mg/dL (reference: 8-32 mg/dL), lactate 16.4 mg/dL (reference: 10.8-18.9 mg/dL), and IgG index 0.74 (reference: <0.5). Cytological examination for malignant cells was negative. Brain T2-weighted MR images showed hyperintense lesions in the bilateral basal ganglia and bilateral frontal lobes especially right side and right parietal subcortical white matter (Fig. 1A). After contrast medium administration, homogeneous enhancement was noted in bilateral basal ganglia especially right side and right parietal region (Fig. 1B). Diffusion weighted imaging (DWI) demonstrated hyperintensity lesions in the right parietal subcortical white matter and right basal ganglion (Fig. 1C). Apparent diffusion coefficient (ADC) image (equal to mean diffusivity) showed hypo-intensity of the right basal ganglion and right parietal area (Fig. 1D). Brain magnetic resonance spectroscopy showed an elevation of choline peak and depressed N-acetylaspartate (Fig. 2A). Brain diffusion tensor image (DTI) showed decreased fractional anisotropy (FA) of the bilateral basal ganglia. (right FA= 0.083 V.s. left FA= 0.111) (Fig. 2B). Brain positron emission tomography (PET) studies with deoxyglucose scan showed no evidence of systemic metastasis. There was no malignancy in the nasopharynx.

A brain biopsy was perfonned from the right basal ganglion area, and pathological examination showed

Table 1. *Differential diagnosis among different neurological diseases by diffusion MRI studies*

Disease	DWI (Trace image)	ADC (MD in DTI)	DTI (FA)
MS[11]	Variable	Variable	Low ↓ [16,17]
Lymphoma[11]	High ↑ ↑	Low ↓ ↓	Low ↓ ↓ [12]
Glioma[11]	Variable	Variable	Low ↓ [12]
Meta (necrotic part)[11]	Low ↓ ↓	High ↑ ↑	
Meta (non-necrotic)[11]	Variable	Variable	Low ↓ ↓ [13]
Abscess[11]	High ↑ ↑	Low ↓ ↓	Mixed ↑ and ↓ [14]

DWI: diffusion weighted imaging, ADC: apparent diffusion coefficient, MD: mean diffusivity, DTI: diffusion tensor images, FA: fractional anisotropy, MS: multiple sclerosis, Meta: metastatic cancer, ↓ : mild decrease, ↓ ↓ : moderate decrease, ↑ : mild increase. ↑ ↑ : moderate increase.

perivascular cuffing with tumor cell infiltration. Medium-sized lymphoid cells contained hyperchromatic nuclei and perinuclear halo. Immunohistochemical stain showed positive staining of CD3 and CD8 but negative staining of CD20, CD30, and CD56 indicating that the tumor cell is T cell lymphoma in origin (Fig. 3).

DISCUSSION

PCNSL usually presents as solitary or multiple homogeneous enhanced lesions mainly located in the supratentorial region, and occasionally ring enhancement may be seen in immune compromised patients[5,6]. If patients have an involvement of the corpus callosum and basal ganglion, brain MRl studies usually reveal a connection between cerebrospinal fluid and the periventricular regions[5]. However, few patients with PCNSL showed unusual leukoencephalopathy[7-9], and some reports showed that T-PCNSL had the tendency with a dispersed presentation without forming a solid mass[7,10]. Therefore, in this situation, it is difficult to make an accurate diagnosis between PCNSL and demyelinating diseases such as acute demyelinating encephalomyelitis, progressive multifocal leukoencephalopathy and multiple sclerosis[7,8], The diffusion-weighted studies of MRI including DWI and ADC are valuable to make a differential diagnosis in this situation. DWI and ADC may indicate the mean degree and magnitude of water diffusion in the brain tissue[11]. Hyper-intense DWI and hypointense ADC imaging may suggest lesions with impairment of water molecule diffusion in the brain tissue similar to the condition of cytotoxic edema, and lymphoma is one of the important differential diagnosis[11]. The patient's MRI images had typical lymphoma pictures including increased DWI and decreased ADC in the right basal ganglion. Increased DWI in the right basal ganglia reflects a decrease of water diffusion (cytotoxic edema) in the lesion and a decreased signal in ADC in lymphoma is probably caused by high cellularity[11,12]. DWI with ADC images are also helpful in differentiation among other neurological diseases including glioma, metastatic tumor, multiple sclerosis and abscess[11,13,14]. Table 1 shows the differential dragnosis among different neurological diseases by diffusion MRl studies. MS has variable signal intensities either hyper-, iso-, or hypointensity in DWI and inreased signal intensity in ADC. The features of MRI might be helpful in differential diagnosis among variable diseases. However hyperintensity in DWI and hypointensity in ADC images can be observed in both lymphoma and MS. Brain biopsy is still warranted to make a definite diagnosis in this situation.

In addition to DWI and ADC, diffusion tensor images (DTI) is also a kind of diffusion MRI image. There are two major parameters in DTI: mean diffusivity (MD) can measure the magnitude of molecule motion (equal to ADC map) and fractional anisotropy (FA) shows degree of directionality in three-dimension particularly for movement of water molecules in the white matter[15]. Decreased FA in DTI indicates the disruption of white matter tracts on lesion site. Decreased FA was found in MS, glioma, metastatic tumor and lymphoma[11,

[15-17]. A recent study showed the FA of primary cerebral lymphoma was significantly lower than glioblastoma[12]. This study suggests that the deceased FA in lymphoma is related to higher cellularity and decreased extracellular space secondary to an attenuated tumor growth[12]. Our patient had a decreased DTI in bilateral basa ganglia especially in the right side which may help us to confirm the dispersed presentation of white matter involvement and feature of forming a solid mass of T-PCNSL[7,10]. However, we would like to emphasize that it is not enough to diagnose PCNSL only by MRI images including DTI, because MS, glioma, metastatic tumor and lymphoma may also present as decreased FA[12,13,15-17]. Most patients with PCNSL require pathological confirmation of the diagnosis except that a few patients may have a diagnosis through cerebrospinal fluid study[18].

Proton magnetic resonance spectroscopy study (MRS) has been used to evaluate demyelinating lesions and lymphoma. In patients with MS, proton MRS may reveal a reduction of N-acetylaspartate and an elevation of choline[19,20]. However, the same findings were also noted in PCNSL[21]. This leads to a challenge in diagnosis of PCNSL only by a proton MRS study.

To our best knowledge, this is a detailed report of T cell PCNSL which complete an extensive survey in the MRI study. In our patient, brain MRI showed several lesions of T2 hyperintensity and contrast enhancement in bilateral basal ganglia. Brain DTI showed decreased FA in the bilateral basal ganglia which may correlate with bilateral extra-pyramidal symptoms. Predominant right frontal lesions may be correlated to a positive right side palmomental reflex. The right cortical and insular region involvement in the MRl images might account for focal seizure in the left arm and mentality changes including memory impairment and agitation.

In Taiwan, there have been series studies of PCNSL in Taiwan[22]. Most of the patients with PCNSL are B cell in origin and T-PCNSL is rare, constituting of 1.8% to 4.6% of CNS lymphoma in western countries[2-4], 8.5% in Japan[23] and 16.7% in Korea. In Taiwan, an incidence of 14% was reported in T-PCNSL[22]. The age, gender, presentation and outcome of T-PCNSL are similar to B cell PCNSL, but T-PCNSL had a tendency to be low-grade in histology[24,25].

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