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Case Report

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A case of progressive multifocal leukoencephalopathy (PML): diffusion-weighted MR imaging findings

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ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is a progressive subacute demyelinating disease caused by neurotropic papova virus, usually in immunocompromised patients. As the number of cases of AIDS increases so close the incidence of PML, the ability to diagnose PML noninvasively is of increasingly importance. A case of PML is presented with conventional magnetic resonance and diffusion-weighted images (DWI) performed at two consecutive months. Conventional MR imagings were performed on a 0.5 T and DWI was performed on 3 T scanner at follow-up.

Key words: progressive multifocal leukoencephalopathy, PML, AIDS, diffusion-weighted MRI.

Introduction

Progressive multifocal leukoencephalopathy (PML) is a subacute demyelinating disease of the central nervous system (CNS) caused by neurotropic papova virus (JC polyoma virüs) [1, 2]. PML was originally described in immunocompromised patients and the disease has been associated with acquired immunodeficiency syndrome (AIDS). PML occurs increasingly in 4% to 7% of patients with AIDS [3, 4].

The disease is usually progressive and prognosis is poor. Only some patients live for up to 2 years after the onset of symptoms, mean survival is 6-9 months [5].

Definitive diagnosis of PML requires brain biopsy. But it is a need to diagnose noninvasively PML early in its course and to assess treatment response. Magnetic resonance (MR) imaging is the preferred diagnostic technique for the evaluation of patients with AIDS who have neurologic symptoms. Characteristic MR imaging abnormalities of PML might facilitate diagnosis and follow-up [6-9].

Although MR findings in patients with PML on conventional MR examinations and also specialized MR techniques such as magnetization transfer (MT) and MR proton spectroscopy have been described [10-12], no diffusion weighted imaging (DWI) finding has been described.

In this report, we present a case of PML with AIDS, clinical status and MRI findings progressed to date in three months despite medical therapy. Conventional MR and DWI findings are presented.

Case Report

A 32- year- old man with human immunodeficiency virus (HIV) for 14 years had a 4-week history of increasing left sided hemiparestesia, ataxic gait, dysarthric speech, coordination disorder. Physical examination revealed dysmetry, dysdiadochinesia and ataxic gait. There was right central facial palsy, and no other motor or sensory deficit. The CD4+ count was 114 cells/mm^3 at the time of PML diagnosis.

PML was diagnosed on the basis of clinical signs, course and typical MR imaging. Brain biopsy was planned, but it couldn't be done due to worsen clinical condition of the patient.

MR imaging was performed by a 0,5 T (Philips, Gyroscan NT Intera T5, Netherlands) imager. MRI showed asymmetrical areas of high signal intensity on T2 TSE-weighted sequences on right cerebellar hemisphere, vermis and bilateral frontal and right temporoparietal subcortical white matter without mass effect and contrast enhancement (Figs. 1A, 1B). Deep gray matter structures were spared. During the following month, despite the use of antiretroviral therapy his clinical status progressed, he developed dysorientation and his memory was impaired. A repeat MR imaging showed progression of the previous findings and extension of the signal abnormalities to the brainstem, mostly the pons. No mass effect or contrast enhancement was observed (Figs. 2A, 2B). Because DWI by 0.5 T scanner was poor in quality, we performed DWI by 3 T scanner (Siemens, Allegra, Germany). ADC (appearent diffusion coefficient) values were calculated on DWI as described elsewere previously [13]. The mean ADC values

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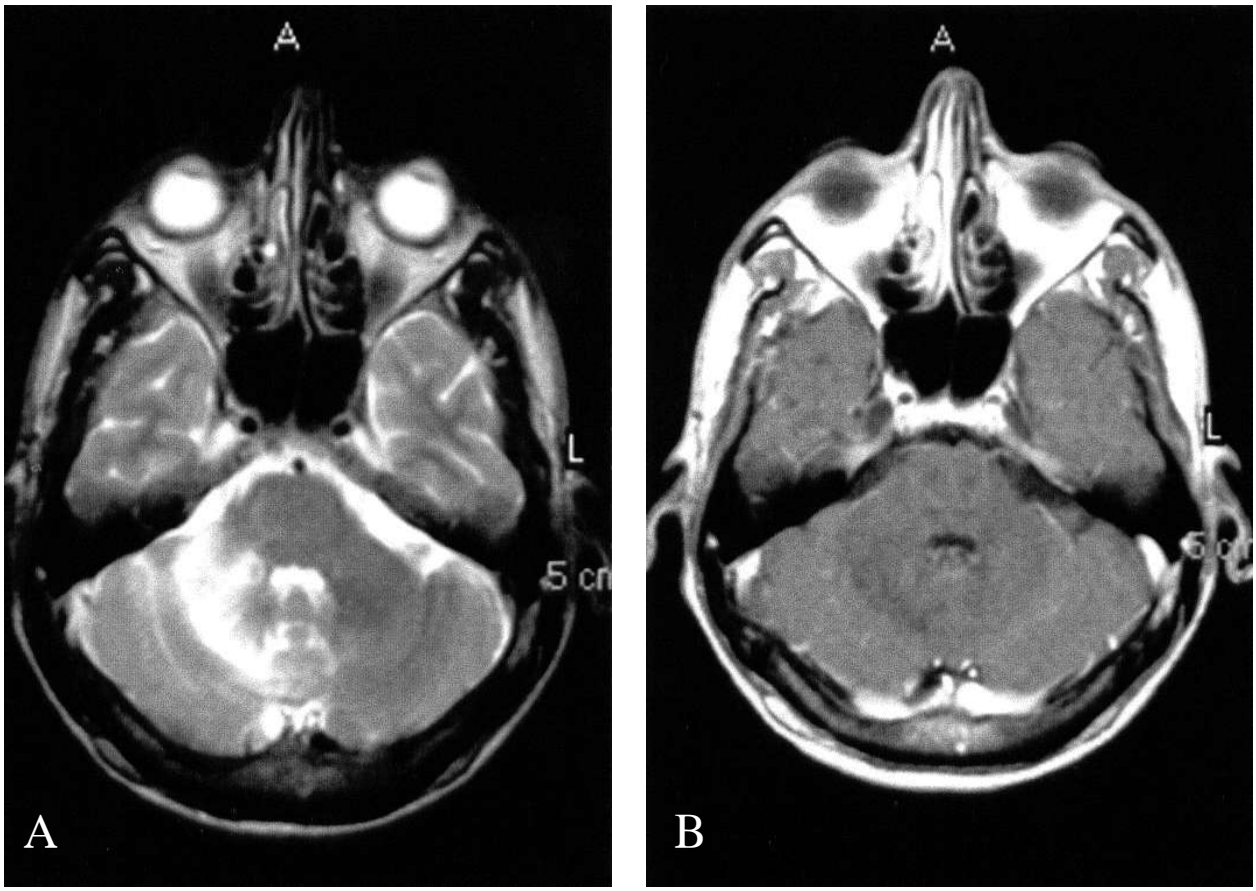

Figure 1 | T2W TSE (TR/TE, 4000/100) image shows lesion at right cerebellar hemisphere that extends to vermis and middle cerebellar pedincle (A). Postcontrast T1W SE (TR/TE, 500/15) image shows no contrast enhancement in the lesion (B).

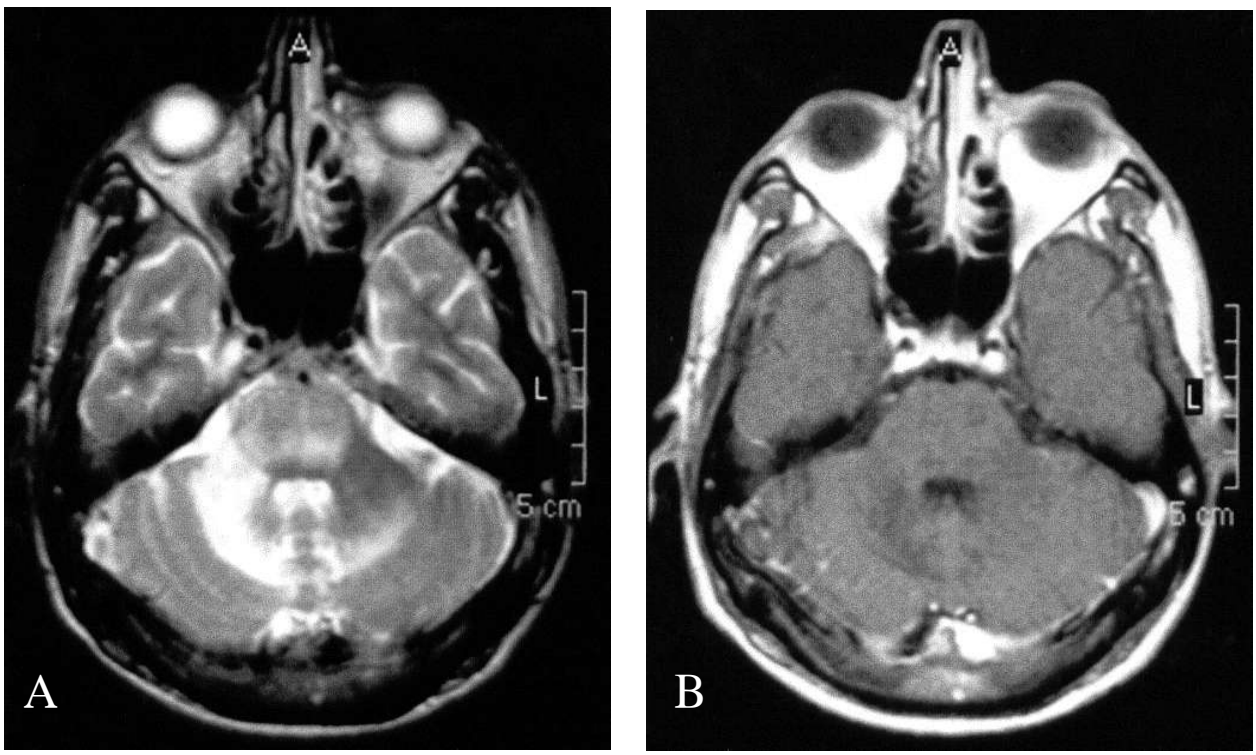

Figure 2 | Two weeks later extension of the nonenhancing lesion to brainstem is shown on T2W image (A), and postcontrast T1W SE images (B).

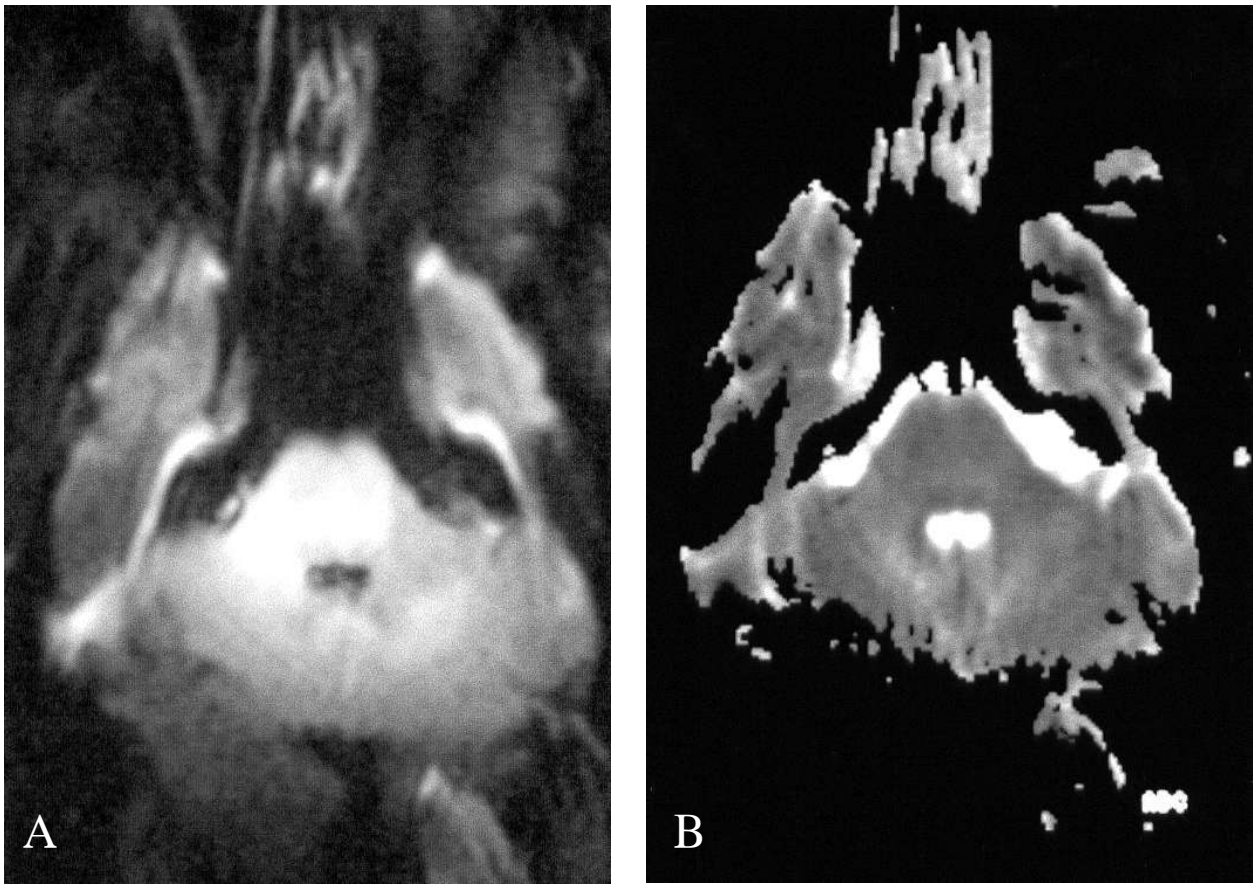

Figure 3 | DWI. Both trace (A) and ADC map (B) reveals high signal intensity of lesion (ADC values in the right middle cerebellar pedincle: 1.26 x 10^{-3} ± 13.2, in the pons: 0.91 x 10^{-3} ± 8.1).

(in the right middle cerebellar pedincle: 1.26 x 10^{-3} ± 13.2, in the pons: 0.91 x 10^{-3} ± 8.1) in the old and new lesions were increased (Figs. 3A, 3B).

The clinical status of the patient failed theraphy and the patient died 2 weeks later; hence no second follow-up MR imaging could be obtained.

Discussion

PML is a demyelinating disease of the brain caused by infection of oligodendrocytes by a papova virus. Since the oligodendrocytes are the cells that produce and maintain the myelin sheaths in the central nervous system, involvement of these cells by the virus explains the demyelinating nature of PML [1, 2].

PML was first described by Astrom et al. in 1958 in association with chronic lymphocytic leukemia and Hodgkin's disease [14]. Since then, PML has been associated with immunocompromised patients, including AIDS. The frequency and mortality of AIDS related PML have dramatically increased [3, 4]. Because there is no effective treatment for PML, the prognosis is poor and survival is usually no longer than 9 months. Recent studies have reported improvement in patients with AIDS associated PML treated with a combination of antiretroviral agents [6, 7].

In patients with AIDS, imaging is important and often helpful in the diagnosis of PML. Recent studies showed characteristic MR abnormalities in AIDS patients with histopatologically confirmed PML and by MR imaging PML could be diagnosed noninvasively [6-9].

MRI usually demonstrates asymmetric areas of increased signal in the white matter on T2 weighted images and decreased signal on T1 weighted images. The parietal lobe is the most commonly involved. Less commonly, there are cerebellar, brainstem and cortical gray matter involvement. Donovan Post et al. showed higher prevalance of cerebellar, brain stem involvement than previously reported [7]. In their series of 47 patients with AIDS who had PML. Whiteman et al. [15] reported involvement of the posterior fossa in 32% of cases.

PML lesions generally do not exhibit any mass effect or contrast enhancement. However, faint, peripheral contrast enhancement has been described [6, 15]. Recently, contrast enhancement has been thought to be the result of an intense imflammatory reaction and found to be one of the predictive factors for prolonged survival [6, 16, 17]. Thuruher et al. [6] suggested that enhancing PML is characteristic of patients who experienced immunological reconstitution during the early phase of theraphy. Our patient had relatively low CD4+ count at the time of the diagnosis. During the retroviral therapy, CD4+ count did not rise and no contrast enhancement was present in the follow-up MR imaging. A mild degree of mass effect associated with PML has been described in the published literature [7, 9]. Another study found a correlation between the presence of a mass effect and shorter survival time [7]. However, Thuruher

et al. [6] mentioned that the development of mass effect in the immediate phase after theraphy might have resulted from transient edema rather than progression of the PML.

In the literature, MT imaging has been used for differential diagnosis of PML and HIV-related white matter lesions in patients with AIDS [10, 11]. However, to date no DWI finding has been described. ADC values have been studied in the normal human brain [13, 18]. Sener [13] found that in the normal white matter ADC ranges were 0.60-1.05 x 10^{-3} mm^2/s, and the mean ADC value was 0.84 ± 0.11 x 10^{-3} mm^2/s. Helenius et al. [18] found that mean ADC values were highest in the cortical gray matter (0.89 x 10^{-3} ± 0.04 mm^2/s), lower in the deep gray matter (0.75 x 10^{-3} ± 0.03 mm^2/s), lowest in the white matter (0.70 x 10^{-3} ± 0.03 mm^2/s). We found increased ADC values in the brainstem and cerebellum. It has been well reported that in multiple sclerosis, the classical common demyelinating disease, lesions may have higher ADC values [19, 20]. Because PML is also a demyelinating disease, PML lesions could lead to greater ADC values compared to the normal brain structures. Other than the better suppression of normal parenchyme and higher resolution of images, we do not expect a different DWI finding of this lesion at a lower field magnet systems such as 1.5 or 1 T scanners. Increased ADC values could be useful in differential diagnosis of other white matter lesions such as lymphoma, toxoplasmosis and encephalitis all of which are seen more frequently in AIDS population, since these lesions may show normal, reduced ADC values [21-23].

References

[1] Berger JR, Concha M. Progressive multifocal leukoencephalopathy: the evolution of a disease one considered rare. Neurovirol. 1995 (1) 5-18.

[2] Brooks BR, Walker DL. Progressive multifocal leukoencephalopathy. Neurol. Clin. 1984 (2) 299-313.

[3] Holman RC, Janssen RS, Buehler JW, Zelasky MT, Hooper WC. Epidermiology of progressive multifocal leukoencephalopathy in the United States: analysis of national mortality and AIDS surveillance data. Neurology. 1991 (41) 1733-1736.

[4] Berger JR, Kasovitz B, Donovan-Post MJ, Dickinson G. Progressive multifocal leucoencephalopathy associated with human immunodeficiency virus: a review of the literature with a report of sixteen cases. Ann. Intern. Med. 1987 (107) 78-87.

[5] Berger JR, Mucke L. Prolonged survival and partial recovery in AIDS- associated progressive multifocal leukoencephalopathy. Neurology. 1988 (38) 1060-1065.

[6] Thurnher MM, Donovan Post MJ, Rieger A, Kleible-Popov C, Loewe C, Schindker E. Initial and follow-up MR imaging findings in AIDS-related progressive multifocal leukoencephalopathy treated with highly active antiretroviral therapy. AJNR Am. J. Neuroradiol. 2001 (22) 977-984.

[7] Post MJ, Yiannoutsos C, Simpson D, Booss J, Clifford DB, Cohen B, McArthur JC, Hall CD. Progressive multifocal leukoencephalopathy in AIDS: are there any MR findings useful to patient management and predictive of patient survival? AIDS Clinical Trials Group, 243 Team. AJNR Am. J. Neuroradiol. 1999 (20) 1896-1906.

[8] Mark AS, Atlas SW. Progressive multifocal leukoencephalopathy in patients with AIDS: appearance on MR images. Radiology. 1989 (173) 517-520.

[9] Thurnher MM, Thurnher SA, Muhlbauer B, Hainfellner JA, Steuer A, Fleischmann D, Trattnig S, Budka H, Schindler E. Progressive multifocal leukoencephalopathy in AIDS: initial and follow-up CT and MRI. Neuroradiology. 1997 (39) 611-618.

[10] Ernst T, Chang L, Witt M, Walot I, Aronow H, Leonido-Yee M, Singer E. Progressive multifocal leukoencephalopathy and human immunodeficiency virus-associated white matter lesions in AIDS: magnetization transfer MR imaging. Radiology. 1999 (210) 539-543.

[11] Dousset V, Armand JP, Lacoste D, Mieze S, Letenneur L, Dartigues JF, Caill JM. Magnetization transfer study of HIV encephalitis and progressive multifocal leukoencephalopathy. Groupe d'Epidemiologie Clinique du SIDA en Aquitaine. AJNR Am. J. Neuroradiol. 1997 (18) 895-901.

[12] Chang L, Ernst T, Tornatore C, Aronow H, Melchor R, Walot I, Singer E, Cornford M. Metabolic abnormalities in progressive multifocal leukoencephalopathy: a proton magnetic resonance spectroscopy study. Neurology. 1997 (48) 836-845.

[13] Sener RN. Diffusion MRI: apparent diffusion coefficient (ADC) values in the normal brain and a classification of brain disorders based on ADC values. Comput. Med. Imag. Graphics. 2001 (25) 299-326.

[14] Astrom KE, Mancall EL, Richardson EP. Progressive multifocal leukoencephalopathy: a hitherto unrecognized complication of chronic lymphatic leukemia and Hodgkin's disease. Brain. 1958 (81) 93-111.

[15] Whiteman MLH, Post MJD, Berger JR, Tate LG, Bell MD, Limonte LP. Progressive multifocal leukoencephalopathy in 47 HIV-seropositive patients: neuroimaging with clinical and pathologic correlation. Radiology. 1993 (187) 233-240.

[16] Berger JR, Levy RM, Flomenhoft D, Dobbs M. Predictive factors for prolonged survival in acquired immunodeficiency syndrome-associated progressive multifocal leukoencephalopathy. Ann. Neurol. 1998 (44) 341-349.

[17] Kotecha N, George MJ, Smith TW, Corvi F, Litofsky NS. Enhancing progressive multifocal leukoencephalopathy: an indicator of improved immune status. Am. J. Med. 1998 (105) 541-543.

[18] Helenius J, Soinne L, Perkio J, Salonen O, Kangasmaki A, Kaste M, Carano RA, Aronen HJ, Tatlisumak T. Diffusion-weighted MR imaging in normal human brains in various age groups. AJNR Am. J. Neuroradiol. 2002 (23) 194-199.

[19] Scanderberg AC, Tomaiuolo F, Umberto S, Nocentini U, Grasso MG, Caltagirone C. Demyelinating plaques in relapsing-remitting and secondary-progressive multiple sclerosis: assessment with diffusion MR imaging. AJNR. 2000 (21) 862-868.

[20] Roychowdhury S, Maldjian JA, Grossman RI. Multiple sclerosis: comparison of trace apparent diffusion coefficients with MR enhancement pattern of lesions. AJNR. 2000 (21) 869-874.

[21] Kupfer MC, Zee CS, Colletti PM, Boswell WD, Rhodes R. MRI evaluation of AIDS-related encephalopathy: toxoplasmosis vs. lymphoma. Magn. Reson. Imaging. 1990 (8) 51-57.

[22] Stadnik TW, Chaskis C, Michotte A, Shabana WM, van Rompaey K, Luypaert R, Budinsky L, Jellus V, Osteaux M. Diffusion-weighted MR imaging of intracerebral masses: comparision with conventional MR imaging and histologic findings. AJNR Am. J. Neuroradiol. 2001 (22) 969-976.

[23] Chang L, Ernst T. MR spectroscopy and diffusion-weighted MR imaging in focal brain lesions in AIDS. Neuroimaging Clin. N. Am. 1997 (7) 409-426.