Original Article

The Diagnostic Value of Brain Magnetic Resonance Imaging in Detecting CNS Diseases Among Advanced AIDS Patients

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Objective To investigate the diagnostic value of brain magnetic resonance imaging in detecting central nervous system diseases among AIDS patients of different levels of T cells.

Methods Total of 164 AIDS patients who did not receive antiviral treatment were divided into 2 groups according to their baseline CD4⁺ T cell counts. Group A had CD4⁺ T cell below or equal to 50 cells/ μ l (n = 81) and group B had CD4⁺ T cells over 50 cells/ μ l (n = 83). All patients underwent brain MRI scan. Imaging analysis and the prevalence of the central nervous system disorders were compared between two groups.

Results Among them 48 cases were found of abnormal brain MRI, group A was higher than group B (35.8% vs. 22.9%) although without statistical significance ($P = 0.065$). Altogether 48 cases were diagnosed as AIDS related central nervous system disorders based on clinical symptoms, signs and laboratory findings. The prevalence of CNS disorders was higher in group A than in group B (41.9% vs. 16.8%) with statistical significance ($P < 0.01$).

Conclusions The patients with CD4⁺ T cell count less than or equal to 50 cells/ μ l had high prevalence of CNS diseases. Brain MRI plays an important role in the diagnosis and differentiation of CNS diseases in advanced AIDS patients. This study suggests patients with low CD4⁺ T cell count ($\leq 50/\mu$ l) should routinely undergo MRI examination.

Key words: Central nervous system; Intracranial diseases; CD4⁺ T cell; Magnetic resonance imaging

Patients with advanced AIDS have a high risk of intracranial opportunistic infections and neoplasms.^{1,2} An autopsy report showed that up to 90% of HIV infected individuals had histopathological changes in the central nervous system (CNS).³ Although the introduction of HAART led to a decrease of central nervous system opportunistic infections, the prevalence of HIV-associated neurocognitive disorder (HAND) is still on the rise.⁴ Thus, early diagnosis of these diseases is important for the clinical management of AIDS patients.

Brain magnetic resonance imaging (MRI) is more sensitive to reveal subtle white matter and meningeal abnormalities than computer tomography

(CT)^{5,6} and has high diagnostic value in the CNS disorders. However, there are few studies on the utility of brain MRI screening to detect intracranial diseases of Chinese AIDS patients, especially for the diagnosis of HAND. This observational study was designed to evaluate the usefulness of brain MRI in screening CNS diseases among advanced AIDS patients with low CD4⁺ T cell count.

METHODS

Study design and participants

An observational study of AIDS patients hospitalized in Shenzhen Third People's Hospital was conducted from June 2011 to May 2013. All patients fulfilled the following inclusion criteria: (1) elder than 18

years old; (2) positive in HIV-Ab test by ELISA and confirmed by Western blot; (3) diagnosed with AIDS according to WHO classification in 2006⁷ and Chinese guideline in 2011.⁸ (4) agreed to undergo brain MRI and finished in clinical practice. Exclusion criteria: did not meet the above criteria or had begun antiretroviral treatment.

The study patients (n = 164) were classified into two groups according to their initial CD4⁺ T cell counts. Patients of group A (N = 81) had initial CD4⁺ T cell count $\leq 50/\mu\text{l}$ and those of group B (N = 83) had initial CD4⁺ T cell count > 50 cells/ μl . The study protocol was approved by the Institutional Review Board and the Ethics Committee of Shenzhen Third People's Hospital. Written informed consent was obtained from all participants.

Brain MRI scan

MRI scanning was performed on a 1.5-Tesla MR scanner (Philips, Achieva). T1-weighted images covering the whole brain were acquired with a spin echo sequence in an axial orientation: repetition time = 400 ms, echo time = 2.0 ms, thickness = 7.0 mm, gap = 1 mm, field of view = 173 mm $\times$ 230 mm. T2-weighted images were acquired with a fast spin echo sequence in an axial orientation: repetition time = 370 ms, echo time = 90 ms, thickness = 7.0 mm, gap = 1 mm, field of view = 173 mm $\times$ 230 mm. Gd-DTPA enhancement MRI scan was performed with a dose of 0.1 mmol/kg in an axial, sagittal, coronal orientation.

Diagnosis of the central nervous system disorders

(1) the clinical signs and symptoms as fever, headache, vomiting, conscious disturbance, seizures, etc. (2) the blood and cerebrospinal fluid (CSF) culture, cytological and serologic testing for all kinds of infections including HSV, CMV, *Toxoplasma gondii*, *Staphylococcus*, *candida albicans*, *M. tuberculosis*, *Cryptococcus*, JCV, etc. (3) CNS lymphoma was assessed based on the MRI findings and further confirmed by histological diagnosis through fine needle aspiration or excisional biopsy of enlarged lymph nodes or bone marrow biopsy.

Diagnosis of HAND

HAND is assessed using combination of neuropsychological tests (cognitive complains questionnaire, the Montreal cognitive assessment, international HIV dementia scale), brain MRI features (cerebral atrophy, widened cortical sulci, enlarged ventricles, reduced grey matter and white matter volumes) and tests on CSF (HIV RNA positive).

Statistical analysis

Data were analyzed using SPSS. Baseline characteristics between two groups were compared using the Student's *t* test and chi-square (χ^2) for continuous and categorical variable, respectively. Prevalence of abnormal MRI and intracranial disorders was calculated and compared in two groups with the χ^2 test. *P* value < 0.05 was considered significant.

RESULTS

The general information of patients

The study included 164 hospitalized patients who underwent brain MRI scan in clinical practice, of whom 81 patients' CD4⁺ T cell count ≤ 50 cells/ μl and 83 patients' CD4⁺ T cell count > 50 cells/ μl . The median CD4⁺ T cell count was 51.5 cells/ μl (IQR 14-182), 14 cells/ μl (IQR 5-33) in group A and 177 cells/ μl (IQR 93-304) in group B, respectively. The patients in group A had higher HIV-1 viral load (5.46 log₁₀/ml, IQR 5.0-5.8) than group B (5.46 log₁₀/ml, IQR 5.0-5.8; *P* < 0.001). There was no statistical significant difference in median age and sex (*P* = 0.95, *P* = 0.33) between two groups (Table 1).

Prevalence of the abnormal MRI

All study patients have undergone brain MRI scan and the MRI diagnosis were fulfilled by more than two experienced radiologist. Among the 164 study patients, prevalence of the abnormal MRI was 29.2% (n = 48), Abnormality in 29 of 81 from group A (35.8%) was higher than 19 of 83 from group B (22.9%), but there was no statistically significant difference (*P* = 0.065). Subgroup analysis the type of abnormal MRI, brain atrophy is the most popular

type in 26 of 48 abnormal scan (53%). The prevalence of brain atrophy in group A was still higher than group B (21% vs. 10.8%), but the difference was not significant ($P = 0.075$). The other types of abnormal MR image ($n = 37$) included lacunar cerebral infarction ($n = 10$), one or more round spots ($n = 6$), multiple flake spots ($n = 15$), confluent lesion ($n = 4$), structural distortions ($n = 2$). In addition, some scans showed more than one type of abnormality. For example, 15 other type abnormal MRI scans were found in combination with brain atrophy (Table 2).

Prevalence of the central nervous system disorders in the patients

Based on the patient clinical signs and symptoms, laboratory finding, neuroimaging and outcome of diagnostic treatment, 48 of 164 patients were diagnosis of CNS disorder with a prevalence of 29.3%. The cases included HIV-1 associated neurocognitive disorders ($n = 19$), toxoplasmic encephalitis ($n = 6$), cryptococcal meningitis ($n = 6$), tuberculous meningitis and encephalitis ($n = 3$), neurosyphilis ($n = 3$), fungal meningitis ($n = 1$), cerebral infarction ($n = 4$), PML ($n = 2$), CNS lymphoma ($n = 2$), unknown ($n = 2$). The prevalence of CNS diseases in patients of group A was 41.9% (34/81) and 16.8% (14/83) in patients of group B. The CNS diseases, including HAND and other intracranial diseases, were more prevalent in patients with low CD4 cells than in patients with high CD4⁺T cells ($P < 0.01$) (Table 3).

DISCUSSION

A growing clinical application of antiviral drugs has greatly reduced medical morbidity and mortality of AIDS patients.⁹ However, many patients who were unaware of their HIV status had already been in advanced AIDS. A variety of opportunistic infections, especially intracranial diseases make the diagnosis complex and the mortality rate high. The prevalence (29.3%) of the CNS diseases in our study is higher than most of previous studies in China (10-20%),^{10, 11} possibly because of the difference of the study samples. The patients in our study were newly admitted in hospital without ART treatment. Most of

their CD4⁺T cell counts were less than 200/ μ l (the median is 51.5/ μ l) and about half were less than 50/ μ l. The patients with CD4⁺T count < 200 / μ l had been reported to be a high risk to intracranial diseases.¹ The prevalence (32%) of patients with CD4⁺T count < 200 / μ l in the study in Japanese by Nishijima et al¹² is similar to our result.

Additionally, HIV is a neurotropic virus which invades the central nervous system (CNS) through infecting monocytes and macrophages from the time of primary infection and causes a variety of neurologic dysfunctions and neurocognitive impairments generally termed HAND.¹³ It has been estimated that neurocognitive impairment occurred in 20% to 50% of all individuals infected with HIV.¹⁴⁻¹⁷ In the early HAND, patients may not have any clinical symptoms, or mild impairment of cognitive function. The diagnosis of HAND is based on using combination of neuropsychological tests, brain MRI features and tests on CSF. In this study, the prevalence of HAND is 11.6%, which is similar to the study by Nishijima et al¹², but is lower than most related studies. There are several possible causes. First, many early HAND patients without obviously clinical symptoms and signs could be ruled out because brain MRI scanning is expensive and physician in charge made selection bias. Second, a part of HAND patients who developed intracranial opportunistic infections were ruled out. Third, the HAART era model of lower frequencies of HIV-associated dementia and increased prevalence of milder forms of HAND is not suitable for our study, in which the all study subjects were HAART naïve and in advanced AIDS. Despite this, HAND was still the most main type of AIDS related CNS diseases (19/48, 39.6%) in our study. HAND has posted an important challenge to the fight against AIDS.

Early diagnosis of HAND has posted an important challenge against AIDS. MRI has a high sensitivity in identifying lesions of the central nervous system. Brain MRI features in HIV/AIDS patients usually demonstrate widened cortical sulci, enlarged ventricles, reduced gyri, the low signal in T1WI and the high signal in T2WI, the lesion around ventricles and absence of space occupying lesion and strengthening signal.¹⁸⁻²⁰ Our results showed that

Table 1. Clinical and demographic information on the study patients

	Total (n = 164)	Group A (CD4 $\leq$ 50, n = 81)	Group B (CD4 > 50, n = 83)	P value
Age, years ^a	37 (31-48)	37 (30-48)	37 (32-48)	0.95
Gender, male (%)	142 (86.6)	68 (84.0)	74 (89.2)	0.33
CD4 cell count (/ μ l) ^a	51.5 (14-182)	14 (5-33)	177 (93-304)	< 0.01
HIV RNA in plasma (log ₁₀ copies/ml) ^a	5.2 (4.9-5.6)	5.46 (5.0-5.8)	5.13 (4.7-5.5)	< 0.01
Detectable HIV RNA in CSF ^b	77/98 (78.6)	56/63 (88.9)	21/35 (60)	NA
Homosexual contact (%)	76 (46.3)	39 (48.1)	37 (44.6)	0.65

Notes : ^a Data are presented as the median (IQR);

^b CSF data were available for 98 participants (63 in group A, 35 in group B); NA: not available

Table 2. The prevalence of MRI abnormality in the study patients

	Total (n = 164)	Group A (CD4 $\leq$ 50, n = 81)	Group B (CD4 > 50, n = 83)	P value
Total abnormality/n (%)	48/164 (29.3)	29/81 (35.8)	19/83 (22.9)	0.069
Brain atrophy/n (%)	26/164 (15.9)	17/81 (21.0)	9/83 (10.8)	0.075
Only atrophy	11	7	4	
Combined atrophy	15	10	5	
Others/n (%)	37/164 (22.6)	22/81 (27.2)	15/83 (18.0)	0.164
Lacunar cerebral infarction	10	5	5	
One or more round spots	6	4	2	
Multiple flake spots	15	9	6	
Confluent lesion	4	2	2	
Structural distortions	2	2	0	

Table 3. The prevalence of the central nervous system diseases in the study patients

	Total (n = 164)	Group A (CD4 $\leq$ 50, n = 81)	Group B (CD4 > 50, n = 83)	P value
The CNS disorders/n (%)	48/164 (29.3)	34/81 (41.9)	14/83 (16.8)	< 0.01
HAND/n (%)	19/164 (11.6)	14/81 (17.2)	5/83 (6)	0.024
Others/n (%)	29/164 (17.7)	20/81 (24.7)	9/83 (10.8)	0.023
Toxoplasmic encephalitis	6	4	2	
Cryptococcal meningitis	6	5	1	
Tuberculous meningitis and encephalitis	3	2	1	
Neurosyphilis	3	2	1	
Candida albicans meningitis	1	1	0	
Cerebral infarction	4	2	2	
PML	2	2	0	
Malignant lymphoma	3	2	1	
Unknown	1	0	1	

Notes: CNS: central nervous system; HAND: HIV associated neurocognitive disorders; PML: progressive multifocal leukoencephalopathy;

nearly 30% of all study patients had brain MRI abnormal changes, 35.8% of the patients with CD4 counts less than 200 cells/ μ l did so. Together with the results of other tests, brain MRI improved our ability for the final diagnosis of the CNS diseases in AIDS patients.

Our study is limited in several ways. Firstly, some AIDS hospitalized patients without HAART can't enter the observation due to the lack of brain MRI examination, especially those in critically ill patients or patients without neurological symptom. Secondly, other clinical profiles including drug addiction, alcoholism, HCV infection, anemia, malnutrition and other factors may affect the brain function were incomplete. Thirdly, the number of study patients is slightly less, which caused difference in the incidence of MRI abnormalities between two groups fail to reach the statistical standard although close to.

In conclusion, AIDS related CNS diseases have a devastating effect on HIV-positive individuals, especially those in whom diagnosis is delayed or concurrent infection with more than one CNS disease. Mortality is often high and thus early detection of HIV and associated CNS diseases is urgent. Magnetic resonance also plays an important role in the diagnosis and differentiation of primary and secondary CNS diseases in advanced AIDS patients and we suggest patients with low CD4⁺ T cell count (less than 50/ μ l) should routinely undergo MRI scan even though they have no neurological signs and symptoms.

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