Comparison and Correlation of Magnetic Resonance Imaging and Clinical Severity in Nonhuman Immunodeficiency Virus Patients with Cryptococcal Infection of Central Nervous System

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Abstract

Background: The incidence of cryptococcal meningitis among immunocompetent patients increases, especially in China and imaging plays an important role. The current study was to find the correlation between magnetic resonance imaging (MRI) manifestation and clinical severity in nonhuman immunodeficiency virus patients with cryptococcal infection of central nervous system (CNS).

Methods: A total of 65 patients with CNS cryptococcal infection from August 2014 to October 2016 were retrospectively included in this study. All the patients had MRI data and clinical data. The patients were divided into two groups according to whether the patients were confirmed with identifiable underlying disease. Comparison and correlation of MRI and clinical data in both groups were investigated using independent sample *t*-test, Chi-square test, Mann-Whitney test and Spearman rank correlation analysis.

Results: In all 65 patients, 41 cases (41/65, 63.1%; Group 1) had normal immunity and 24 cases (24/65, 36.9%; Group 2) had at least one identifiable underlying disease. Fever, higher percentage of neutrophil (NEUT) in white blood cell (WBC), and increased cell number of cerebral spinal fluid (CSF) were much common in patients with underlying disease (Group 1 vs. Group 2: Fever: 21/41 vs. 21/24, $\chi^2 = 8.715$, $P = 0.003$; NEUT in WBC: 73.15% vs. 79.60%, $Z = -2.370$, $P = 0.018$; cell number of CSF: 19 vs. 200, $Z = -4.298$, $P < 0.001$; respectively). Compared to the patients with normal immunity, the lesions are more common in the basal ganglia among patients with identifiable underlying disease (Group 1 vs. Group 2: 20/41 vs. 20/24, $\chi^2 = 7.636$, $P = 0.006$). The number of the involved brain areas in patients with identifiable underlying disease were well correlated with the number of cells and pressure of CSF ($r = -0.472$, $P = 0.031$; $r = 0.779$, $P = 0.039$; respectively).

Conclusions: With the increased number of the involved brain areas in patients with identifiable underlying disease, the body has lower immunity against the organism which might result in higher intracranial pressure and more severe clinical status.

Key words: Central Nervous System; Clinical Status; Cryptococcal Meningitis; Immunity; Magnetic Resonance Imaging

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Introduction

Cryptococcal meningitis (CM) is a fungal infection and inflammation of the meninges, which has a high mortality and morbidity around the world in despite of advances in antifungal treatment.[1] Although it is commonly seen in immunosuppressive patients, the incidence of CM among immunocompetent patients increases, especially in China.[2-6] *Cryptococcus neoformans* (*C. neoformans*) is a type of encapsulated fungus and unicellular yeast which is small enough to pass through the meningeal capillary and causes cerebral dissemination.[1] The predilection of cryptococcal invasion of central nervous system (CNS) may be related to abundant nutrients in the brain and lack of serum inhibitor of cerebral spinal fluid (CSF). The enzymes produced by the organism can lyse the pial epithelium and lead to parenchymal invasion. The morbidity of cryptococcal infection in CNS among immunocompetent patients has increased during recent years.[1,4,5] Early diagnosis and treatment are correlated with a reduced morbidity and good prognosis.

The most common appearances of CNS cryptococcal infection in patients with human immunodeficiency virus (HIV) are meningoencephalitis, cryptococcoma, dilated Virchow-Robin spaces, dirty cranial base and so on.[6-13] However, leptomeningitis or meningoencephalitis is much more common in HIV patients with immune reconstitution.[8-10,12] The pathogenesis and imaging appearances of CNS cryptococcal infection largely depend on the patients' immunity. Different immunology, localization and stages of CNS cryptococcosis may result diverse imaging findings.[13,14] Therefore, patients without immunodeficiency may show different imaging appearances. Until now, there are limited literatures that reported the imaging appearances of CNS cryptococcal infection among immunocompetent patients and majority of them are case reports.[14,15] One study with 19 cases of cryptococcal infection showed that leptomeningitis and intraventricular cystic lesions were more commonly seen than intraparenchymal involvement in immunocompetent patients.[16] Another similar study with 18 cases found that the parenchymal involvement, meningitis, enlarged Virchow-Robin space and ventricular lesions are equally common among immunocompetent patients.[17] However, more imaging data should be collected in order to have a detailed discussion on the appearances of CNS cryptococcal infection among immunocompetent patients.

Some literatures reported the comparison of clinical characterization, laboratory examination, treatment response and outcome between non-HIV patients with predisposing factors and patients without.[2-6] The patients with predisposing factors are prone to have abnormal imaging findings. However, they did not demonstrate the imaging characterization and the relationships with clinical information.

In the current study, we hypothesized that there are different distribution of the CNS cryptococcal infection among non-HIV patients with and without identifiable underlying disease and the number of brain areas involved is correlated with clinical severity. We collected magnetic resonance imaging (MRI) data of CNS cryptococcal infection from a large cohort of non-HIV patients that were enrolled from tertiary hospitals in different regions of China. The imaging characteristics and clinical data were analyzed to investigate the correlation in different clinical severity between patients with and without identifiable underlying disease.

Methods

Ethical approval

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Ethics Committee of Beijing Youan Hospital. As a retrospective study and data analysis was performed anonymously, this study was exempt from the informed consent from patients.

A total of 125 patients with CNS cryptococcal meningoencephalitis diagnosed according to clinical and laboratory examination between August 2014 and October 2016 were recruited in this study. The data were collected from 10 tertiary hospitals for infectious diseases from different cities of China and were analyzed at Department of Radiology in two hospitals of Tianjin First Central Hospital and Youan Hospital Affiliated to Capital Medical University, China.

All the patients were HIV-negative with initial onset of cryptococcal meningoencepgalitis, and presented with at least one of the following findings: (1) isolated *C. neoformans* during CSF culture; (2) positive CSF cryptococcal antigen (Ag) titer; and (3) positive CSF India ink staining. Only patients with available conventional and contrast enhanced MRI were included in this study. And the MR data was collected within 2 weeks before or after the clinical diagnosis of cryptococcal meningoencephalitis.

Based on the inclusion criteria, 65 patients were enrolled, including 42 males and 23 females, with mean age of 48 ± 15 years ranging from 14 to 71 years. The patients were divided into two groups: One group with identifiable predisposing disease (Group 2, n=24) and the other group without (Group 1, n=41). Clinical data, such as symptoms duration, presence of fever, headache, predisposing factors, blood routine examination, CSFs and cranial pressure, were also collected.

Among 24 CM patients (Group 2) with identifiable underlying diseases, the most common disease was hepatitis B (14/24, 58.3%), other diseases included hypertension, diabetes mellitus, tuberculosis, rheumatoid arthritis, silicosis, hematological disease and multiple organ failure. Table 1 shows detailed information.

All of the MR data were collected from 3.0 Tesla units (Trio Tim, Siemens AG, Erlangen, Germany). The sequences included sagittal spin-echo T1-weighted, turbo spin echo T2-weighted, fluid attenuated inversion recovery, echo-planar

Table 1: Demographical and clinical data of patients with and without predisposing factors

Variable	Group 1		Group 2		Statistics	*P*
	n	Results	*n*	Results		
Age (years)	41	49.7 ± 14.5	24	47.1 ± 15.9	0.641*	0.524
Sex (male/female)	41	26/15	24	16/8	0.070†	0.791
Fever	41	21	24	21	8.715†	0.003
Headache	41	35	24	22	0.557†	0.456
Symptom duration (days)	41	45.58 ± 11.47	24	32.49 ± 5.88	1.125*	0.256
WBC ($\times 10^9$/L)	40	9.66 (6.48, 12.73)	23	9.60 (7.20, 13.08)	−0.114‡	0.909
NEUT (%)	40	73.15 (9.49, 82.50)	23	79.60 (73.20, 89.30)	−2.370‡	0.018
EOS (%)	30	0.49 (0.05, 1.58)	19	0.50 (0.10, 1.30)	−0.031‡	0.975
BASO (%)	28	0.20 (0.05, 0.48)	18	0.30 (0.10, 0.53)	−0.712‡	0.476
CSF						
Cell	28	19.00 (8.18, 100.00)	23	200.00 (122.00, 397.00)	−4.298‡	<0.001
Glucose (mmol/L)	37	2.45 (1.09, 7.00)	13	1.39 (0.88, 2.39)	−1.714‡	0.087
Protein (g/L)	39	1.26 (0.54, 3.00)	16	0.91 (0.57, 2.11)	−0.612‡	0.541
Chloride (mmol/L)	39	118.40 (110.00, 125.50)	14	116.10 (114.28, 120.53)	−0.515‡	0.607
LDH (U/L)	33	107.00 (35.50, 137.00)	4	89.50 (12.79, 159.73)	−0.245‡	0.807
Pressure (mmH_2O)	13	270.00 (227.50, 357.50)	11	299.00 (180.00, 360.00)	−0.174‡	0.862

Values are presented as mean ± SD or median (P25, P75). *n* is the total number of the cases in each group. Because laboratory test indicators had missing values, so the case number of different indicators is difference in the same group. **t* values; †χ^2 values; ‡*Z* values. 1 mmH_2O = 0.0098 kPa. WBC: White blood cell; NEUT: Neutrophils; EOS: Eosinophilic cells; BASO: Basophilic granulocyte; CSF: Cerebral spinal fluid; LDH: Lactate dehydrogenase; SD: Standard deviation; Group 1: Patients without predisposing factors; Group 2: Patients with predisposing factors.

diffusion-weighted imaging (DWI-EPI, b = 1000 s/mm^2). Gadolinium-DTPA was injected via antecubital vein at a dose of 0.1 mmol/kg magnevist (Bayer, Germany) with a 20 ml saline flush. The injection rate was set at 2 ml/s using a power injector.

Images analysis

The images were analyzed by two neuroradiologists with more than 10 years of experience. They were both informed that all the patients had definite diagnosis of CNS cryptococcal infection. The distribution of lesions, such as frontal, parietal, temporal, occipital lobe, basal ganglia, brain stem and cerebellum, was recorded. The contrast-enhanced manifestation, such as meningitis, meningoencephalitis, ependitis or abscess, were also recorded. Pseudocysts, dilated Virchow-Robin spaces and hazy brain base were recognized. The accompanying changes of brain, including hydrocephalus, infarction and leukoariosis were also noted during images analysis. Some of the uncommon appearances, such as intracranial cyst were also recorded.

Statistical analysis

The statistics analysis of the data was performed by SPSS 17.0 (SPSS Inc., Chicago, IL, USA). The distribution of age between two groups was compared using two independent sample *t*-test. The distribution of gender and clinical symptoms between two groups were analyzed by Chi-square test. Mann-Whitney test was used to compare the differences of blood examination and CSF results. The number of involved brain areas, the incidence of meningitis/encephalitis, ependitis, abscess, Virchow-Robin spaces, pseudocyst, dirty brain base and incidence of hydrocephalus, leukoariosis, infarction were compared using Chi-square test or Fisher *t*-test (if the statistical number <5) between two groups. The relationships between the number of involved brain areas and the index of clinical blood examination or CSF results were analyzed using spearman rank correlation analysis or partial correlation analysis in each group. A value of $P < 0.05$ was considered to be statistically significant.

Results

In all 65 patients with CNS cryptococcal infection, 41 cases (41/65, 63.1%; Group 1) had normal immunity and 24 cases (24/65, 36.9%; Group 2) had identifiable underlying disease. No statistical differences of age and gender were found between the two groups (all $P > 0.05$). Fever was much more commonly seen in patients with underlying disease (Group 1 vs. Group 2: Fever: 21/41 vs. 21/24, $\chi^2 = 8.715$, $P = 0.003$). The percentage of neutrophil (NEUT) in WBC and the cell number of CSF in patients with underlying disease were much higher than the measures in immunocompetent patients (Group 1 vs. Group 2: NEUT in WBC: 73.15% vs. 79.60%, $Z = -2.370$, $P = 0.018$; cell number of CSF: 19 vs. 200, $Z = -4.298$, $P < 0.001$; respectively). Other clinical information, such as headache and laboratory examination, including total white blood cell (WBC), eosinophilic cells (EOS) (%), basophilic granulocyte (BASO) (%) didn't show statistical differences between the two groups (all $P > 0.05$). There was no significant difference in other factors of CSF including glucose, protein, chloride, lactic dehydrogenase and cranial pressure between the two groups (all $P > 0.05$). The detailed information were summarized in Tables 1 and 2.

Compared to the patients without identifiable underlying disease, the lesions were more commonly distributed in

the basal ganglia in patients with identifiable underlying disease (20/41 vs. 20/24, $\chi^2 = 7.636$, $P = 0.006$; Table 3) and the most common lesions were dilated Virchow-Robin spaces [Figure 1]. Other brain areas, such as parietal lobe and frontal lobe, temporal lobe, occipital lobe, brain stem and cerebellum, were equally involved in both groups ($P > 0.05$; Table 3). Meningitis/encephalitis [Figure 2], dirty basal base [Figure 3], dilated Virchow-Robin spaces and pseudocysts are the main findings of the two groups and equally seen in these two groups ($P > 0.05$). The other less common appearances included: ependitis, abscess, intracranial big cyst. Tables 3 and 4 showed detailed information about the distribution and imaging appearances of the two groups.

Table 2: Predisposing factors in patients with cryptococcal infection of CNS

Predisposing factors	*n*	Frequency (%)
Hepatitis B	14	21.5
Diabetes mellitus	3	4.6
Tuberculosis	2	3.1
Rheumatoid arthritis	1	1.5
Silicosis	1	1.5
Hematological disease	1	1.5
Multiple failure	1	1.5
Total	28	43.1

CNS: Central nervous system.

Table 3: The distribution of lesions in patients with and without predisposing factors

Distribution of lesions	Group 1 ($n = 41$)	Group 2 ($n = 24$)	χ^2	*P*
Basal ganglia	20	20	7.636	0.006
FR	12	6	0.138	0.711
FL	12	6	0.138	0.711
PR	12	4	1.109	0.255
PL	14	6	0.595	0.441
OR	10	4	0.534	0.465
OL	10	6	0.003	0.956
TR	10	3	1.448	0.247
TL	9	4	0.264	0.607
Cerebellum	10	5	0.108	0.743
Brainstem	4	1	0.666	0.414

FR: Right frontal lobe; FL: Left frontal lobe; PR: Right parietal lobe; PL: Left parietal lobe; OR: Right occipital lobe; OL: Left occipital lobe; TR: Right temporal lobe; TL: Left temporal lobe; Group 1: Patients without predisposing factors; Group 2: Patients with predisposing factors.

The accompanying brain findings in both two groups were leukoariosis (1/41; 0/24), infarction (12/41; 10/24) and hydrocephalus (3/41; 5/24). No statistical differences were found between the two groups ($P > 0.05$, Table 4).

The number of involved brain areas in patients with identifiable underlying disease were well correlated with the number of cells ($r = -0.472$, $P = 0.031$) and pressure of CSF ($r = 0.779$, $P = 0.039$; Figure 4). No correlations were found between the percentage of NEUT, EOS, BASO, content of CSF-glucose, protein, chloride and the number of involved brain areas in both groups (all $P > 0.05$, Table 5).

Discussion

In the current study, a large cohort of patients with CNS cryptococcal infection were collected. There are three major findings. First, the lesions in patients with identifiable underlying disease were more commonly distributed in the basal ganglia and the most common lesion was Virchow-Robin space. Second, the incidence of fever, higher percentage of NEUT in WBC, increased number of cells of CSF in patients with underlying disease were much more common than those in normal immune patients. Third, the number of the involved brain areas in patients with identifiable underlying disease were negatively correlated with the number of CSF cells and positively correlated with the pressure of CSF.

Lots of literatures have reported the MRI signs of CM in CNS among immunosuppressive patients.[7-10,18,19] In this study, the involvement of basal ganglia is much more common in patients with identifiable underlying disease and

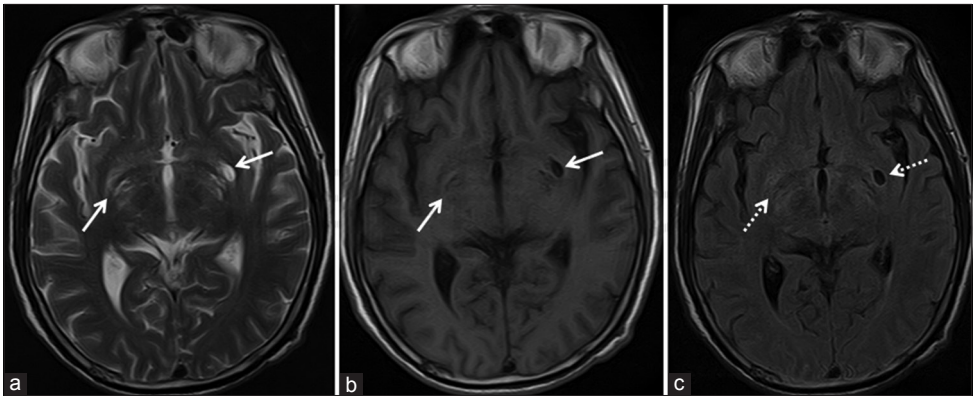

Figure 1: Typical dilated Virchow-Robin spaces of magnetic resonance imaging. A 60-year-old man complaint fever with a history of hepatitis B type virus. Multiple dot-like long T1 and long T2 lesions were demonstrated at the bilateral basal ganglia (a and b) (solid arrows). The lesions are symmetrical and suppressed on FLAIR sequence (c) (dotted arrows). FLAIR: Fluid attenuated inversion recovery.

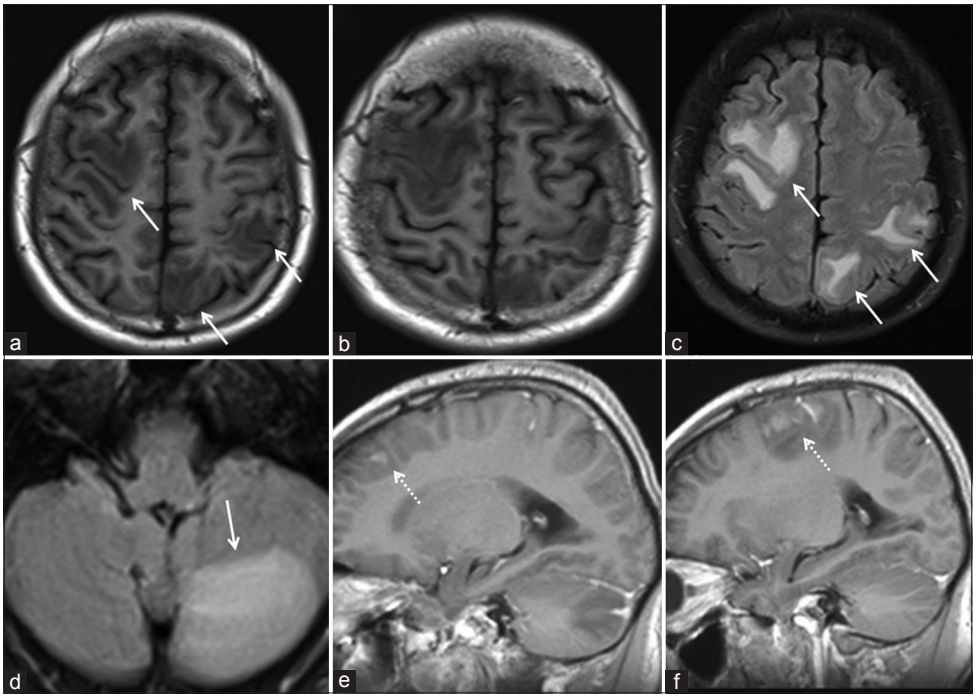

Figure 2: Meningitis and encephalitis involved bilateral frontal and parietal lobe and also left cerebellum in magnetic resonance imaging. A 53-year-old man complaint of fever with normal immunity. Multiple patchy like lesions were detected on bilateral frontal and parietal lobe and also left cerebellum. The lesions showed hypointensity on T1WI (a and b) and hyperintensity on FLAIR (c and d) (solid arrows). Linear contrast enhancement could been seen inside the lesions (e and f) (dotted arrows). FLAIR: Fluid attenuated inversion recovery.

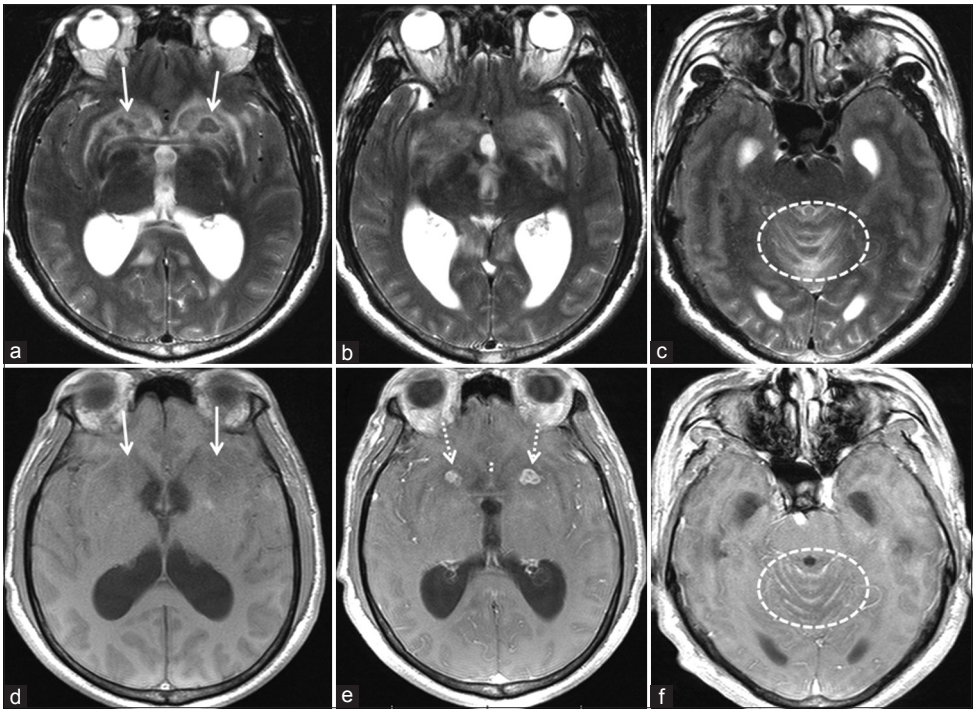

Figure 3: Meningitis of cerebellum and dirty brain base in magnetic resonance imaging. A 53-year-old man with a history of hepatitis B type virus. Cryptococcus were detected positive. Symmetrical patchy lesions with poorly defined boundaries were shown in the bilateral basal ganglia. Cerebellum was shown swelling and the cerebellar sulcus was shown to be narrowed. The lesions manifested patchy hyperintensity on T2WI (a-c), low intensity on T1WI (d) (solid arrows). Nodular contrast enhancement (dotted arrows) had been seen in the basal ganglia (e) and linear contrast enhancement (dotted circles) seen in cerebellum (f).

majority of the lesions were manifested as Virchow-Robin space. In a study of 35 cases of HIV pediatric patients with CM, the most common imaging appearance was dilated Virchow-Robin space (44.4%).[20] Lesions in basal ganglia are primarily spread through blood. Depending on the numbers of fungal organism and mucinous material,

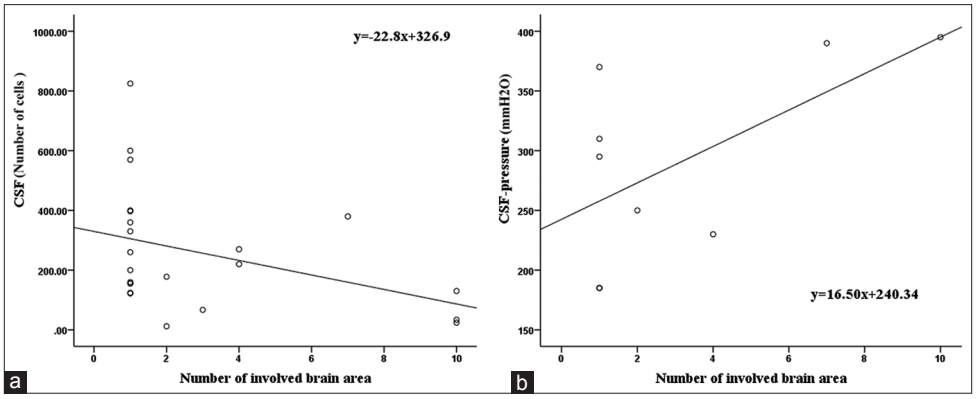

Figure 4: Correlation between involved brain areas and the number of cells and pressure of CSF. (a) The number of involved brain areas in patients with identifiable underlying disease are negatively correlated with the number of cells of CSF ($r = -0.472$, $P = 0.031$) and (b) positively with pressure of CSF ($r = 0.779$, $P = 0.039$). CSF: Cerebrospinal fluid; 1 $mmH_2O = 0.0098$ kPa.

Table 4: The imaging characterization in patients with and without predisposing factors

Imaging appearances	Group 1 ($n = 41$)	Group 2 ($n = 24$)	χ^2	*P*
Meningitis/encephalitis	17	13	0.983	0.321
Ependitis	1	1	0.243	0.697
Abscess	0	1	1.735	0.188
VRS	8	12	6.606	0.010
Pseudocyst	3	0	1.841	0.175
Dirty brain base	7	5	0.142	0.706
Accompanying findings				
Hydrocephalus	3	5	2.562	0.109
Infarction	12	10	1.039	0.308
Leukoariosis	1	0	0.595	0.441

VRS: Virchow-Robin spaces; Group 1: Patients without predisposing factors; Group 2: Patients with predisposing factors.

Table 5: Correlations between the involved brain areas and clinical laboratory examination

Parameter	Group 1 ($n = 41$)		Group 2 ($n = 24$)	
	r	*P*	*r*	*P*
WBC	0.040	0.805	0.377	0.092
NEUT (%)	0.069	0.674	0.040	0.862
EOS (%)	−0.129	0.499	0.455	0.058
BASO (%)	0.159	0.418	0.077	0.776
CSF				
Cell	0.026	0.896	−0.472	0.031
Glucose	−0.098	0.565	−0.400	0.222
Protein	−0.045	0.785	−0.067	0.821
Chloride	0.020	0.905	0.317	0.315
LDH	0.156	0.387	NA	NA
Pressure	0.121	0.655	0.779	0.039

Group 1: Patients without predisposing factors; Group 2: Patients with predisposing factors; NA: The number of CSF-LDH in Group 2 (only four cases) failed to meet the requirements of statistics. WBC: White blood cell; NEUT: Neutrophils; EOS: Eosinophilic cells; BASO: Basophilicgranulocyte; CSF: Cerebral spinal fluid; LDH: Lactate dehydrogenase.

imaging appearances such as Virchow-Robin spaces, pseudocysts and dirty brain base might be observed.[7-9] Less contrast enhancement of lesions could be seen in the basal ganglia due to slight inflammatory reaction and fewer plasmocytes infiltration in patients with predisposed disease. In patients with identifiable underlying disease, immune system is compromised and the body does not have enough ability against the organism and therefore mild or no inflammatory response can be formed.

Other imaging findings, such as meningitis or meningoencephalitis, were also identified in the study, but no differences were found between the two groups. Although the immunity of patients with underlying diseases such as hepatitis B, hypertension, etc., was decreased, but different to the immunodeficiency in patients with HIV. Without immunodeficiency, the host has good immune response to the cryptococcal organism and much more inflammatory reaction against the pathogenesis of CM was observed.[21] Increased activity of the complement system of cerebrospinal fluid in patients without HIV indicates good host immune response against the cryptococcal infection.[22] Some literatures reported that meningeal enhancement is the most common appearances in HIV patients with immune reconstruction treatment.[8,9,12] Meningitis or meningoencephalitis on imaging can be a promising indication for early lumbar puncture andtreatment for the patients.[23]

Hydrocephalus, infarction and leukoariosis are equally seen in patients with and without underlying disease. The mechanism for the hydrocephalus may be related with organisms depositing within the choroid plexus or superficial leptomeninges.[24,25] Acute or old infarction and leukoariosis can also be seen in patients with CM which might be the result of inflammation of perforating arteries due to the fungal invasion along perivascular spaces.[10,18]

In the present study, 36.9% (14/65) of patients with CNS CM had identifiable underlying diseases. The percentage is similar to other reports.[2-5] The incidence of fever, the percentage of NEUT in WBC, the number of CSF cells in patients with underlying disease are much higher than those in normal immune patients. One report did not show any differences in blood and CSF measures between two groups.[20] Another report showed higher WBC count of CSF in patients without underlying disease.[21] The differences between our study and other reports maybe related with patients' age and severity of

underlying disease. Among the underlying diseases, hepatitis B virus is the most common organism apart from HIV, which is consistent with another report.[21]

Number of CSF cells and pressure of CSF increased in both groups compared to normal range of value. In patients with identifiable underlying disease, as the number of the involved brain areas increased, the number of CSF cells decreased and the pressure of CSF increased. However, this tendency was not observed in patients with normal immunity. In patients with underlying disease, the low immunity along with larger area of involved brain tissue by CM was observed, as the body cannot have enough inflammatory response to defend the organism.[21,23,26-29] Some other reports also showed increased number of CSF cells and pressure of CSF in patients with or without HIV infection and patients with or without predisposed disease.[23,26-29] Intracranial hypertension is one of the most severe complications in patients with CM, which had high morbidity and mortality.[30,31] Approximately 50% of patients with CM have intracranial pressure over 200 mmH_2O.[31] Previous literatures reported that increased pressure of CSF is one of risk factors related to the prognosis of CM. It has been reported that higher pressure of CSF is associated with much poorer prognosis in some cases.[32] Therefore, relieving the intracranial pressure is one of the most important treatments.

The main limitation of the current paper is that it is a retrospective study, and therefore some clinical data are not complete. Further studies with strict prospective and follow-up design are needed to investigate the effects of different immune status on the imaging manifestation and prognosis of the disease. Some of the identifiable underlying diseases should be carefully analyzed to make sure the etiology of the CM. Some of the imaging appearances should be combined with the patients' history to make sure if it is complications and accompanying disease.

In conclusion, the lesions of CM in patients with identifiable underlying disease are more commonly distributed in the basal ganglia and the most common lesion is dilated Virchow-Robin space. Incidence of fever, the percentage of NEUT in WBC, the number of cells of CSF in patients with identifiable underlying disease are much higher than those in normal immune patients. The higher number of the involved brain areas in patients with identifiable underlying disease is associated with the decreased immune response. The higher intracranial pressure might indicate more severe clinical status.

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Conflicts of interest

There are no conflicts of interest.

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中枢神经系统隐球菌感染的非HIV患者磁共振成像与临床严重程度的比较及相关性

摘要

背景：隐球菌性脑膜炎在免疫功能正常的患者中的发病率增加，尤其是在中国。影像学在其中发挥着重要作用。本研究旨在寻找中枢神经系统隐球菌感染的非人类免疫缺陷病毒（HIV）患者中MR影像表现与临床严重程度之间的相关性。

方法：回顾性分析并纳入2014年8月至2016年10月共65例CNS隐球菌感染患者。 所有患者均具有MR成像数据和临床资料。 根据患者是否确诊患有可识别的潜在疾病，将患者分为两组。 采用独立样本*t*检验，卡方检验，Mann-Whitney检验和Spearman相关分析，研究两组MR成像与临床资料的差异及相关性。

结果：65例患者中，41例（41/65,63.1％；第1组）具有正常免疫力，24例（24/65,36.9％；第2组）至少有一种潜在疾病。 发热，中性粒细胞在白细胞计数（WBC）中高百分比，脑脊液（CSF）细胞数增加在具有基础疾病的患者中更为常见（正常免疫力患者组和具有基础疾病的患者组: 第1组 vs. 第2组； 发热:21/41 vs 21/24, χ^2=8.715,p=0.003; 中性粒细胞: 73.15% vs. 79.60%, Z=-2.370, p=0.018; 脑脊液细胞数: 19 vs. 200, Z=-4.298, p<0.001）。 与免疫正常的患者相比，具有潜在疾病患者的基底神经节中的病变更为常见第1组 vs. 第2组: 20/41 vs. 20/24, χ^2=7.636,p=0.006）。 具有潜在疾病的患者中颅内病灶的数量与细胞数量和脑脊液压力密切相关（r=-0.472, p=0.031; r=0.779, p=0.039）。

结论：在具有潜在疾病的患者中，随着颅内病灶的数量增加，机体的免疫力下降，可能导致更高的颅内压和更严重的临床状态。