Unique Cerebrospinal Fluid Profiles of Patients With Human Immunodeficiency Virus- Associated Cryptococcal Meningitis With a Ventriculoperitoneal Shunt : A Retrospective Cohort Study

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Abstract

Background: The long-term complications of ventriculoperitoneal shunting in patients with human immunodeficiency virus-associated cryptococcal meningitis remain unclear. We conducted a case-control study investigating the long-term effects of ventriculoperitoneal shunting in patients with human immunodeficiency virus-associated cryptococcal meningitis.

Methods: Between January 2011 and December 2019, 112 patients with human immunodeficiency virus-associated cryptococcal meningitis from our hospital were enrolled in this retrospective cohort study. Of those, 30 (26.8%) patients underwent ventriculoperitoneal shunting (VPS group); the remaining (n = 82; 73.2%) were included in the non-VPS group. Survival was estimated using the Kaplan–Meier method. Univariate and multivariate Cox regression analyses were performed to identify factors associated with ventriculoperitoneal shunting.

Results: The VPS group (n=21) had lower cerebrospinal fluid glucose (2.51 ± 0.81 vs. 3.16 ± 0.48 mmol/L; $P=0.002$) and higher cerebrospinal fluid protein levels ($1.37 [0.83–1.49]$ vs. $0.49 [0.49–0.49]$ g/L; $P=0.011$) than did the non-VPS group (n=21). Intracranial pressure decreased from 400 (375–450) to 164 (145–172) mmH₂O in the VPS group (log-rank, $P<0.001$). The 24-week cumulative survival rates in the VPS and non-VPS groups were 100.0% and 79.8%, respectively ($P=0.035$). The misdiagnosis rates of tuberculous meningitis were 28.6% and 0.0%, respectively ($P=0.008$).

Conclusions: Ventriculoperitoneal shunting decreased the intracranial pressure and 24-week mortality in patients with human immunodeficiency virus-associated cryptococcal meningitis, but significantly increased cerebrospinal fluid protein levels, leading to a higher misdiagnosis rate of tuberculous meningitis. Physicians should be aware of these changes in the cerebrospinal fluid profiles of patients with human immunodeficiency virus-associated cryptococcal meningitis with a ventriculoperitoneal shunt.

Background

Among patients with human immunodeficiency virus (HIV)-associated cryptococcal meningitis (HCM), the incidence of intracranial hypertension is > 50% [1]. Furthermore, high intracranial pressure (HICP; >350 mmH₂O) is associated with increased mortality in patients with HCM and intracranial hypertension [1–4]. Thus, control of HICP is a critical determinant of the outcome of patients with HCM with HICP [5]. Daily lumbar puncture and permanent ventriculoperitoneal shunt (VPS) placement are important in the management of patients with HICP. In particular, VPS placement is successfully used in the treatment of patients with uncontrollable intracranial pressure (ICP), rapidly relieving symptoms of HICP and significantly reducing mortality. In addition, excess cerebrospinal fluid (CSF) in the ventricles and the fungal polysaccharide load can be decreased by using a VPS, significantly improving patient outcomes. Thus, VPS placement is the preferred treatment for patients with persistent HICP after failure to control increased ICP with conservative measures.

Although VPS placement significantly increases the survival rate of patients with HICP, the use of a VPS in people living with HIV (PLHIV) remains controversial. For example, severe immunodeficiency in PLHIV may increase the risk of local infection after VPS placement, blockage of the device owing to a high fungal load, and peritoneal seeding of cryptococci from the draining compartment [6, 7]. Some patients may develop postoperative infections [8]. More importantly, the long-term complications of VPS placement in patients with HCM remain unclear. Therefore, this study aimed to describe the long-term effects of VPS placement on the CSF profiles and outcomes of Chinese patients with HCM.

Methods

Study Cohort and Patient Enrolment

We aimed to describe the long-term effects of VPS placement on the CSF profiles and outcomes of Chinese patients with HCM. Between January 2011 and December 2019, 112 patients with HCM from our hospital were enrolled in this retrospective cohort study. Of those, 30 (26.8%) patients underwent VPS placement (VPS group) and 82 (73.2%) did not undergo VPS placement (non-VPS group). The following criteria were used to determine the eligibility of patients with HCM for VPS placement: i) nadir ICP ≥ 300 mmH₂O, ii) persistent neurological signs or impaired mentation with an enlarged ventricle on computed tomography (CT)/magnetic resonance imaging (MRI), and iii) provision of consent for surgery by the patient or patient's relatives. Five patients in the VPS group and 42 in the non-VPS group whose follow-up records were unavailable were excluded. Therefore, 25 (38.5%) patients in the VPS group and 40 (61.5%) in the non-VPS group were enrolled in our study. After case-control matching for sex and age at a 1:1 ratio, 21 patients in the VPS group and 21 in the non-VPS group were included. The patient selection process is described in Fig. 1.

Diagnostic Criteria

Patients were diagnosed with cryptococcal meningitis (CM) if they fulfilled at least one of the diagnostic criteria from our previous study [9]: i) a positive CSF culture of *Cryptococcus neoformans*; ii) positive India ink staining of cryptococci in the centrifuged CSF sediment; iii) encapsulated yeast cells in brain tissue, observed using Gomori-methenamine silver and/or periodic acid-Schiff staining; and iv) a positive cryptococcal antigen test result using CSF samples.

Disseminated cryptococcosis was defined as the presence of *Cryptococcus neoformans* in more than one organ [9]. Cryptococci were counted as described in our previous study [9]. Briefly, 1 mL of CSF was collected and centrifuged at 3000 rpm for 10–15 minutes. The sediment (approximately 100 μ L) was mixed with a small drop of India ink. A large coverslip was applied over 100 μ L of the mixture on a glass slide and pressed gently to obtain a thin mount. The slide was scanned under low-power magnification in reduced light using a microscope; we switched to a high-power field (HPF) for counting, if cryptococcal capsules were found, using the following formula:

Cryptococcal count (cells/HPF) = (total number of cryptococcal capsules in 10 HPFs) / 10

Therapeutic Approaches

CM was treated in three phases: i) induction therapy with amphotericin B (0.7–1.0 mg/kg/day) plus 5-formylcytosine (100 mg/kg/day) for 2–4 weeks; ii) consolidation therapy with fluconazole (400–800 mg/day) for 8 weeks; and iii) maintenance therapy with fluconazole (200 mg/day) for at least 6 months.¹⁰ A routine lumbar puncture was performed to assay CSF profiles and ICP. Mannitol and furosemide were administered to reduce increased ICP in patients with ICP < 300 mmH₂O, whereas a VPS was used to control the opening pressure in patients with ICP ≥ 300 mmH₂O. A lumbar puncture was performed every 1–2 weeks after VPS placement to monitor CSF-related changes. Highly active antiretroviral therapy (HAART) was initiated after 2 weeks of antifungal therapy. Follow-up lasted for 24 weeks after the patients were discharged.

Laboratory Tests

Routine blood tests, biochemical tests, and CSF assays (opening pressure, white blood cell [WBC] count, glucose level, protein level, India ink staining, and culture results) were performed at admission and at each follow-up visit. Two experienced consultant neuroradiologists assessed the brain CT and MRI findings independently and blindly.

Follow-Up and Collection of Clinical Data

Data on the patients' characteristics (sex, body mass index [BMI], blood test results, imaging examination results, treatments received, and follow-up) were obtained from the hospital's electronic medical record system. The median time from the initiation of anticytotoxic therapy to VPS placement was 7 days. In the VPS group, the week before VPS placement was considered Week 0, and the week during which VPS placement was performed was considered Week 1. The first week of antifungal treatment in the non-VPS group was considered Week 0. Patients were followed-up for 24 weeks. Records at Weeks 0 (W0), 1 (W1), 2 (W2), 4 (W4), 12 (W12), and 24 (W24) were used for analysis.

Statistical Analyses

Continuous normally distributed variables are presented as means ± standard deviations. Continuous non-normally distributed variables are presented as medians (interquartile ranges). Categorical variables are presented as numbers of cases (percentages). Continuous variables were compared using the Student's *t*-test or Mann–Whitney *U* test, whereas categorical variables were compared using the χ^2 test or Fisher's exact test. CSF profile data at W24 and W0 of the VPS and non-VPS groups were compared using the paired *t*-test or Wilcoxon test. Survival was analyzed using the Kaplan–Meier method. To identify potential factors associated with VPS placement, covariates were first analyzed using univariate analysis. Covariates with *P* < 0.1 in the univariate analysis were included in the multivariate Cox regression analysis using the forward stepwise (likelihood ratio) selection method. Covariates (potential risk factors for VPS placement) included sex (male vs. female), age (< 50 vs. ≥ 50 years), cryptococemia (yes vs. no), CD4 count (< 30 vs. ≥ 30 cells/mm³), WBC count (< 4 vs. ≥ 4 × 10⁹/L), lactate dehydrogenase

level (< 220 *vs.* ≥220 U/L), ICP (< 350 *vs.* ≥350 mmH₂O), VPS placement (yes *vs.* no), neuroimaging abnormalities (yes *vs.* no), CSF WBC count (< 4 *vs.* ≥4×10⁶/L), CSF glucose level (< 2.5 *vs.* ≥2.5 mmol/L), CSF chlorine level (< 120 *vs.* ≥120 mmol/L), and CSF protein level (< 0.45 *vs.* ≥0.45 g/L). Statistical analyses were performed using IBM SPSS 23.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism (version 8.0; GraphPad Software, La Jolla, CA, USA). *P* < 0.05 was considered statistically significant.

Ethics Approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants. All analyzed data were anonymized.

Results

Baseline Characteristics

The mean age was 35.57 ± 9.24 years in the VPS group and 35.52 ± 9.28 years in the non-VPS group (*P* = 0.987). The proportions of patients in each group with fever, headache, and vomiting are shown in Table 1. Patients in the VPS group had a higher incidence of seizures (3 [14.3%] *vs.* 0 [0.0%]; *P* = 0.072), and a higher frequency of abnormal head CT/MRI findings (11 [52.4%] *vs.* 5 [23.8%]; *P* = 0.057), than did those in the non-VPS group. There was no significant difference in the frequency of disseminated cryptococcosis between the groups (*P* = 0.190). Patients in the VPS group had significantly higher ICP than did those in the non-VPS group (400 [340–450] *vs.* 270 [170–375] mmH₂O; *P* = 0.002). The biochemical profile of CSF was compared between the groups. CSF chlorine and glucose levels were higher in the VPS group, while the CSF protein level was higher in the non-VPS group. The demographic characteristics and laboratory test results are shown in Table 1.

Table 1

Differences in the Clinical Features of Patients with HCM Between the VPS and Non-VPS Groups

Factors	VPS Group (n = 21)	Non-VPS Group (n = 21)	P- Value
Age (years)	35.57 ± 9.24	35.52 ± 9.28	0.987
Sex (male), n (%)	20 (95.2)	20 (95.2)	1
Interval from symptom onset to the initiation of anticytotoxic therapy (days)	10 (7–24)	12 (8–26.5)	0.473
Proportion of disseminated cryptococcosis, n (%)	5 (23.5)	9 (42.9)	0.190
Head CT/MRI abnormalities, n (%)	11 (52.4)	5 (23.8)	0.057
Clinical manifestations, n (%)			
Fever	14 (66.7)	16 (76.2)	0.495
Headache	19 (90.5)	17 (81)	0.378
Vomiting	12 (57.1)	12 (57.1)	1
Disturbance of consciousness	1 (4.8)	1 (4.8)	1
Vision loss	2 (9.5)	0 (0)	0.147
Hearing loss	1 (4.8)	0 (0)	0.311
Seizures	3 (14.3)	0 (0)	0.072
Blood test results			
WBC (×10 ⁹ /L)	5.1 (4.0–7.9)	3.9 (3.6–55.5)	0.031
LDH (U/L)	226 (156–305)	265.1 (215–385)	0.128
CD4 (/μL)	14.0 (7.5–37.0)	27.0 (10.5–36.5)	0.450
Alkaline phosphatase (U/L)	83 (59–97)	73 (59–97.5)	0.571
Cholinesterase (U/L)	7,620 ± 2,074.4	6,590.1 ± 1,449.18	0.070
C-reactive protein (mg/L)	7.7 (3.21–21.6)	10.4 (4.1–24.75)	0.497

CM, cryptococcal meningitis; CSF, cerebrospinal fluid; HCM, HIV-associated cryptococcal meningitis; HIV, human immunodeficiency virus; HPF, high-power field; ICP, intracranial pressure; LDH, lactate dehydrogenase; VPS, ventriculoperitoneal shunt; WBC, white blood cell.

Factors	VPS Group (n = 21)	Non-VPS Group (n = 21)	P-Value
First CSF assay			
ICP (mmH ₂ O)	400 (375–450)	270 (170–375)	0.002
Glucose (mmol/L)	3.11 ± 1.02	2.47 ± 0.78	0.026
Chlorine (mmol/L)	118.29 ± 4.55	115.27 ± 6.26	0.082
Total protein (g/L)	0.56 (0.39–0.70)	0.73 (0.50–0.84)	0.122
WBC count (×10 ⁶ /L)	2 (1–12.5)	10 (1–31)	0.193
Cryptococcus <i>neoformans</i> cells/HPF	5 (2–6)	2 (2–5)	0.189
CM, cryptococcal meningitis; CSF, cerebrospinal fluid; HCM, HIV-associated cryptococcal meningitis; HIV, human immunodeficiency virus; HPF, high-power field; ICP, intracranial pressure; LDH, lactate dehydrogenase; VPS, ventriculoperitoneal shunt; WBC, white blood cell.			

Changes in the CSF Profile

Fever, headache, and vomiting improved significantly in both groups ($P < 0.001$). The ICP values at W0 and W24 in the VPS group were 400 (375–450) and 164 (145–172) mmH₂O, respectively ($P < 0.001$). Conversely, there was no significant change in ICP between W0 and W24 in the non-VPS group (270 [170–425] vs. 204 [204–204] mmH₂O; $P = 0.58$). The CSF glucose level decreased from 3.12 ± 1.02 mmol/L at W0 to 2.51 ± 0.81 mmol/L at W24 in the VPS group ($P = 0.020$), whereas it increased from 2.62 ± 0.55 mmol/L at W0 to 3.16 ± 0.48 mmol/L at W24 in the non-VPS group ($P = 0.002$). Conversely, the CSF protein level increased from 0.56 (0.39–0.70) g/L at W0 to 1.37 (0.83–1.49) g/L at W24 in the VPS group ($P = 0.001$), whereas it decreased from 0.73 (0.50–0.84) g/L at W0 to 0.49 (0.49–0.49) g/L at W24 in the non-VPS group ($P = 0.011$). While the CSF chlorine level increased from 114.51 ± 5.91 mmol/L at W0 to 121.19 ± 4.13 mmol/L at W24 in the non-VPS group ($P = 0.001$), there was no significant improvement in CSF chlorine levels between W0 and W24 in the VPS group. There was a significant decrease in cryptococcal count in both groups ($P = 0.001$ for the VPS group; $P = 0.002$ for the non-VPS group) after 24 weeks of antifungal treatment. Additionally, the CSF WBC count increased only in the VPS group ($P = 0.022$). Changes in the CSF profile between the two groups are shown in Fig. 2 and Table 2.

Table 2
Changes in Clinical Symptoms After 24 Weeks of Follow-Up in the VPS and Non-VPS Groups

Factor	VPS Group			Non-VPS Group		
	Baseline (n = 21)	24 Weeks of Follow-Up (n = 20)	P- Value	Baseline (n = 21)	24 Weeks of Follow-Up (n = 16)	P- Value
Clinical manifestations, n (%)						
Fever	14 (66.7)	0 (0)	< 0.001	16 (76.2)	0 (0)	< 0.001
Headache	19 (90.5)	5 (25.0)	< 0.001	17 (81.0)	2 (12.5)	< 0.001
Vomiting	12 (57.1)	0 (0)	< 0.001	12 (57.1)	1 (6.3)	< 0.001
Altered mental status	1 (4.8)	0 (0)	0.323	1 (4.8)	0 (0)	0.376
Visual symptoms	2 (9.5)	1 (5.0)	0.578	0 (0)	1 (6.3)	0.245
Auditory symptoms	1 (4.8)	0 (0)	0.323	0 (0)	0 (0)	1
Convulsions	3 (14.3)	1 (5.0)	0.317	0 (0)	0 (0)	1
Cerebrospinal fluid						
Glucose (mmol/L)	3.12 ± 1.015	2.51 ± 0.81	0.02	2.62 ± 0.55	3.16 ± 0.48	0.002
Chlorine (mmol/L)	118.29 ± 4.55	118.81 ± 3.30	0.54	114.51 ± 5.91	121.19 ± 4.13	0.001
Protein (g/L)	0.56 (0.39– 0.70)	1.37 (0.83– 1.49)	0.001	0.73 (0.50– 0.84)	0.49 (0.39– 0.49)	0.011
WBC (×106/L)	2.0 (1.0– 12.5)	15.0 (2.5–32.7)	0.022	10.0 (1.0– 31.0)	16.1 (16.1– 16.1)	0.840
ICP (mmH ₂ O)	400 (375– 450)	164 (145–172)	< 0.001	270 (170– 425)	204 (204– 204)	0.58
<i>Cryptococcus neoformans</i> count (/HPF)	5 (2–6)	1.7 (1–2)	0.001	2 (2–5)	1.5 (1.5–1.5)	0.002
HCM, HIV-associated cryptococcal meningitis; HPF, high-power field; ICP, intracranial pressure; VPS, ventriculoperitoneal shunt; WBC, white blood cell.						

Treatment and Outcomes

The number of patients treated with amphotericin B was 17 of 21 (81.0%) in the VPS group and 19 of 21 (90.5%) in the non-VPS group ($P = 0.663$). Integrase strand transfer inhibitor-containing HAART regimens were used for 12 of 21 (57.12%) patients in the VPS group and 4 of 16 (25%) patients in the non-VPS group ($P = 0.093$). In both groups, some patients developed CM after HAART initiation (VPS group vs. non-VPS group: 2 of 21 [9.5%] vs. 5 of 21 [23.5%]; $P = 0.41$).

Of note, 6 of 21 (28.6%) and 0 of 21 (0.0%) patients were misdiagnosed with tuberculous meningitis in the VPS and non-VPS groups, respectively ($P = 0.008$). In addition, 12 of 19 (63.2%) patients in the VPS group and 1 of 16 (6.3%) patients in the non-VPS group used corticosteroids at W24 for immune reconstitution inflammatory syndrome (IRIS; $P = 0.001$).

There was no difference in the frequency of neuroimaging abnormalities between the groups before antifungal therapy initiation (VPS group vs. non-VPS group: 11 of 21 [52.4%] vs. 5 of 21 [23.8%]; $P = 0.057$); however, the improvement rate of neuroimaging abnormalities in the VPS group was significantly higher than that in the non-VPS group (8 of 11 [72.7%] vs. 0 of 5 [0.0%]; $P = 0.026$).

Twenty-Four-Week Mortality and Risk Factors Associated with VPS Placement

Four patients died in the non-VPS group; no patient died within the 24-week follow-up. The cumulative survival rate was 79.8% for patients in the non-VPS group and 100.0% for patients in the VPS group (log-rank, $P = 0.035$; Fig. 3A). Intracranial hypertension was observed in three of the four cases involving death. Patients were stratified according to ICP: an ICP ≥ 350 mmH₂O was defined as HICP, while an ICP < 350 mmH₂O was defined as non-HICP. The survival duration of patients with HICP increased significantly after VPS placement (log-rank, $P = 0.013$; Fig. 3B). Patients in the non-HICP group had a better prognosis regardless of VPS placement, albeit without statistical significance (log-rank, $P = 0.45$; Fig. 3C). Although patients in the VPS group initially presented with high preoperative ICP and serious conditions, they had a lower mortality rate at W24 than did those in the non-VPS group, especially patients with intracranial hypertension. This indicates that VPS placement is effective in improving clinical outcomes.

In the unadjusted univariate analysis, neuroimaging abnormalities (odds ratio [OR]: 3.52, 95% confidence interval [CI]: 0.941–13.174; $P = 0.062$), WBC count (OR: 3.52, 95% CI: 0.941–13.174; $P = 0.062$), CSF chlorine level (OR: 3.33, 95% CI: 0.925–12.012; $P = 0.066$), CSF protein level (OR: 3.69, 95% CI: 0.819–16.656; $P = 0.089$), and ICP (OR: 0.12, 95% CI: 0.029–0.486; $P = 0.003$) were associated with VPS placement. Only CSF chlorine level (OR: 6.12, 95% CI: 1.116–33.400; $P = 0.037$) and ICP (OR: 0.08, 95% CI: 0.014–0.415; $P = 0.003$) were associated with VPS placement in the multivariate Cox regression analysis.

Discussion

Although VPS placement is one of the most important and effective treatments to increase the survival rate of patients with HCM, and to decrease elevated ICP, its effects on the long-term outcomes of these

patients remain unclear. This was the focus of our study. We found the following results: 1) patients with VPS showed obvious CSF changes, such as decreased CSF glucose levels and increased CSF protein levels; 2) VPS placement effectively decreased HICP and mortality in patients with intracranial hypertension; and 3) the change in the CSF profile after VPS placement led to a higher rate of misdiagnosis of tuberculous meningitis in these patients.

In this study, VPS placement significantly reduced HICP and 24-week mortality; however, there was a higher rate of misdiagnosis of tuberculous meningitis and steroid use in patients in the VPS group. Some studies have indicated that VPS placement could significantly decrease ICP and cryptococcal counts in patients without HIV infection [11–13]. However, there is a paucity of data on the effects of a VPS on the CSF biochemical profiles of patients with HCM. Our study indicated that CSF protein levels and WBC counts increased, while CSF glucose levels decreased, significantly in patients in the VPS group. This is consistent with the findings of previous studies [6, 7, 14]. Moreover, apparent changes in the CSF profiles of patients with HCM and a VPS led to a higher rate of misdiagnosis of tuberculous meningitis, inappropriate corticosteroid use, and increased inappropriate use of antibiotics/anti-tuberculosis drugs [14].

To date, the mechanisms underlying the tuberculous meningitis-like CSF profile in patients with VPS are unclear. First, there may be a predisposition to ‘paradoxical’ IRIS. HCM-related IRIS occurs in two forms: ‘paradoxical’ IRIS and unmasking IRIS. The former is characterized by initial improvement in clinical manifestations after antifungal therapy; however, deterioration occurs because of HAART-mediated immune restoration in patients with HCM. Severe IRIS exacerbates the clinical symptoms and signs of HCM, leading to severe disease [15]. In this study, clinical presentations and CSF profiles improved after VPS placement but were exacerbated after HAART initiation. Therefore, ‘paradoxical’ IRIS may have triggered changes in clinical presentations and CSF profiles. Second, placement of the shunting device may have increased CSF protein levels. Previous studies [16, 17] have suggested that CSF protein levels are increased by the placement of external drainage devices in patients with Alzheimer’s disease and are associated with trauma resulting from ventricular drain insertion. Therefore, we speculated that the placement of an external drainage device may have increased CSF protein levels. Third, the placement of an external drainage device may have stimulated the production of cytokines/chemokines, such as vascular endothelial growth factor, transferrin, and brain-derived protein, in CSF, leading to higher CSF protein levels [17–19].

This study suggested that intracranial hypertension, symptoms, and imaging findings were markedly improved after VPS placement in patients with HCM; however, the rates of misdiagnosis of tuberculous meningitis and corticosteroid use were higher in these patients. These results indicated that VPS placement had a potential impact on CSF profiles with long-term VPS use. To the best of our knowledge, this is the first study to describe the impact of VPS placement on changes in CSF profiles.

This study has some limitations. First, the sample size was small. Second, the precise mechanisms underlying increased CSF protein levels were not fully investigated. Larger studies focusing on the

pathogenesis of increased CSF protein levels after VPS placement are required to obtain more reliable data. A comprehensive understanding of the pathogenesis of increased CSF protein levels after VPS placement will help clinicians make rational decisions regarding the proper management of these patients. Third, our study only included Chinese patients, which may affect the generalizability of our results. International prospective multicenter studies are required to obtain more accurate data.

Conclusions

In conclusion, although VPS placement is effective in controlling intracranial hypertension in patients with HCM, it can result in extremely high CSF protein levels, leading to a higher rate of misdiagnosis of tuberculous meningitis. Physicians should be aware of this unique change in the CSF profiles of patients with HCM with VPS, to reduce misdiagnosis, explore the underlying causes of this phenomenon, reduce the occurrence of such phenomenon, and improve long-term prognosis

Abbreviations

human immunodeficiency virus (HIV)

cryptococcal meningitis (CM)

human immunodeficiency virus-associated cryptococcal meningitis (HCM)

high intracranial pressure (HICP)

ventriculoperitoneal shunt (VPS)

intracranial pressure (ICP)

cerebrospinal fluid (CSF)

people living with HIV (PLHIV)

computed tomography (CT)

magnetic resonance imaging (MRI)

high-power field (HPF)

highly active antiretroviral therapy (HAART)

body mass index (BMI)

immune reconstitution inflammatory syndrome (IRIS)

odds ratio (OR)

confidence interval (CI)

Declarations

Ethics approval and consent to participate

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants. All analyzed data were anonymized.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are included within the article and are available from corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

TR and ZB designed the study. TR, GYZ, and XXK collected the data. ZJS perform the operation. TR analyzed the data. TR and XLJ wrote the manuscript. All authors approved the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Figures

Figure 1

Flowchart of patient selection HCM, human immunodeficiency virus-associated cryptococcal meningitis; VPS, ventriculoperitoneal shunt

Figure 2

Comparison of CSF profiles and ICP between the VPS and non-VPS groups * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. CSF, cerebrospinal fluid; HPF, high-power field; ICP, intracranial hypertension; VPS, ventriculoperitoneal shunt; WBC, white blood cell

Figure 3

Comparison of cumulative survival rates between the VPS and non-VPS groups Comparison of (a) 24-week cumulative survival rates between the VPS and non-VPS groups (log-rank, $P=0.035$), (b) 24-week cumulative survival rates of patients with HICP between the VPS and non-VPS groups (log-rank, $P=0.013$), and (c) 24-week cumulative survival rates of patients without HICP between the VPS and non-VPS groups (log-rank, $P=0.45$). HICP, high intracranial pressure; VPS, ventriculoperitoneal shunt