The clinical characteristics and outcome of cryptococcal meningitis with AIDS in a tertiary hospital in China: An observational cohort study

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Research

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Abstract

Background

We collected the clinical data of hospitalized AIDS patients who complicated with cryptococcal meningitis (CM) in nearly 10 years, to analyze the influencing factors of prognosis and provide help for early identification of severe patients, timely rescue measures and improvement of prognosis.

Methods

The 128 subjects were divided into two groups according to the effective/ineffective clinical treatment. Analyzed and compared the data from various aspects.

Results

119 cases (93.0%) had headache, 109 (85.2%) had fever, 95 (74.2%) had nausea and vomiting, 52 (40.6%) had consciousness disorder. 101 patients (78.9%) were effective in clinical treatment, while 27 (21.1%) were ineffective. Multivariate Logistic regression analysis showed that the occurrence of cerebral herniation increased the risk of poor prognosis by 405 times, and the occurrence of disturbance of consciousness increased the risk of poor prognosis by 4.4 times. However, each week of extension of the course of induction therapy reduced the risk of poor prognosis by 0.683 times, and increased the effective outcome of clinical treatment by 1.5 times. In addition, the prognosis of patients with ventriculoperitoneal shunt or lumbar cisterna shunt decompression was better than that of patients without shunt therapy.

Conclusions

Cerebral hernia and disturbance of consciousness are risk factors for prognosis of AIDS patients with CM, and duration of induction therapy is a protective factor for prognosis. Anticryptococcal therapy with high efficiency and sufficient treatment time during induction period is especially critical for improving prognosis. Shunt decompression therapy may improve the prognosis of patients with AIDS complicated with CM.

1. Background

Nearly 30 years after the emergence of antiretroviral therapy (ART), the central nervous system (CNS) opportunistic infection (OI) is still the main cause of illness and death in patients with AIDS (Acquired Immunodeficiency Syndrome, AIDS) [1]. Human Immunodeficiency Virus (HIV) -related central nervous system infections can be caused by a variety of microorganisms, including Mycobacterium tuberculosis, new cryptococcus, cytomegalovirus, and toxoplasma. Cryptococcal meningitis (CM) is one of the most common causes of AIDS-related deaths in the world[2], and it is also the most common fungal infection of the central nervous system, which is characterized by difficult treatment, high mortality and long course of disease. The increased intracranial pressure is positively correlated with the morbidity and mortality of CM [3]. Initial intracranial pressure $\geq$ 250 mmH_2O was found in 65% of CM patients, and disturbance of consciousness was an independent risk factor for death in CM patients[4]. In this study, clinical data of 128 patients with AIDS complicated with CM hospitalized for nearly 10 years were collected, and prognostic factors were analyzed to provide help for early clinical identification of patients with severe CM, timely rescue measures and improved prognosis.

2. Methods

2.1 Subjects

We collected 128 AIDS patients with CM hospitalized in Beijing Ditan hospital from November 2008 to November 2017.

2.2 Diagnostic criteria

The diagnosis of Acquired Immunodeficiency Syndrome (AIDS) referred to *the Guidelines on HIV/AIDS Diagnosis and Treatment in China (2018 edition)*[5]. All the patients were confirmed to be positive for anti-hiv-1 antibody by Western blot test (WB). The diagnosis of CM referred to *the Expert Consensus on the Diagnosis and Treatment of Cryptococcal Meningitis*[6], on the basis of cerebrospinal fluid (CSF) cryptococcal antigens, smear ink staining and fungal culture.

2.3 Methods

Evaluation criteria for clinical efficacy: □Complete response: meningitis symptoms and signs disappeared, CSF routine and biochemical examination returned to normal, ink staining and fungal culture turned negative; □Partial response: meningitis symptoms and signs improved, CSF routine and biochemical examination improved, ink staining and/or fungal culture turned negative; □Invalid: no improvement in symptoms and signs of meningitis, no improvement in routine and biochemical examination of CSF, still positive in ink staining and/or fungal culture; □Death. The end point of observation was patient discharge. Effective clinical treatment=□+□; Ineffective clinical treatment=□+□. The 128 subjects were divided into two groups and compared in terms of age, symptoms, signs, complications, CSF examination, blood examination, treatment timing, treatment plan and course of treatment during induction period.

2.4 Statistical analysis

SPSS 22.0 software was used for data analysis. The measurement data conforming to the normal distribution were expressed as (X±S), and t-test was used. Non-normal distribution data were statistically described by median and quartile, and non-parametric rank sum test was used. The enumeration data were expressed as examples or percentages and X^2 test was used. Logistic regression analysis was performed on the data between the groups. For all analysis, *p* value <0.05 was considered statistically significant.

3. Results

3.1 General characteristics and outcomes

A total of 128 cases were studied, including 113 males and 15 females, aged 14–74 years, and the median age was 37.5 years (30.25 years, 46.75 years). Among them, 119 cases had headache (93.0%), 109 cases had fever (85.2%), 95 cases had nausea and vomiting (74.2%), 52 cases had disturbance of consciousness (40.6%), and 29 cases had sweating (22.7%).There were 82 cases of neck resistance (64.1%), 41 cases ofeye disease (32.0%), 38 cases of cranial nerve injury (29.7%), 25 cases of pathological signs (19.5%) (Fig. 1). There were 31 cases (24.2%) with cryptococcal pneumonia, 14 cases (10.9%) with tuberculous meningitis, 11 cases (8.6%) with epilepsy, 9 cases (7%) with purulent meningitis, 8 cases (6.3%) with cerebral infarction, 6 cases (4.7%) with optic papillary edema, 6 cases (4.7%) with deafness, 4 cases (3.1%, 2 deaths) with cerebral hernia, and 3 cases (2.3%) with hydrocephalus.

The subjects were divided into three groups according to the CSF pressure measurement: 25 patients (19.5%) with a pressure of < 180mmH_2O, 38 patients (29.7%) with a pressure of 180-250mmH_2O, and 65 patients (50.8%) with a pressure of > 250mmH_2O. There were 128 cases (100%) positive for CSF cryptococcus antigen, 105 cases (82.0%) positive for CSF ink staining, and 75 cases (58.6%) positive for CSF fungal culture. There were 125 cases (97.7%) with positive blood cryptococcus antigen and 67 cases (52.3%) with positive blood fungal culture. CD4 + T lymphocyte count 1 ~ 571cells/ul, median 22.5cells/ul (9.25cells/ul, 47cells/ul); The serum HIVRNA load ranged from 0 to 2,832,144 copies/ml, with a median of 68,466.5 copies/ml (18,765.5copies/ml, 186,018.5copies/ml). Among the 128 CM patients, 32 had started ART before starting anti-cryptococcal therapy, with ART duration ranging from 1–56 weeks, with a median duration of 8 weeks (2.25 weeks, 14.75 weeks). The subjects in the induction phase of anti-cryptococcus treatment included: 8 cases (6.3%) of amphotericin B (AmB) ± 5-fluorocytosine (5-FC), 57 cases (44.5%) of fluconazole (FLU) ± 5-FC, 4 cases (3.1%) of voriconazole, 39 cases (30.5%) of mixed regimens and 20 cases (15.6%) of non-standard treatment. The median duration of induction period was 5 weeks (3 weeks, 10 weeks).

The course of CM at admission ranged from 1 to 156 weeks, with a median of 4 weeks (3 weeks, 8 weeks). Hospital stay ranged from 1 day to 210 days, with a median of 20 days (7 days, 41 days). Symptoms disappeared in 33 peoples (25.8%), with a median time of 2 weeks (1.5 weeks, 3 weeks), 77 patients (60.2%) improved, the median time was 3 weeks (2 weeks, 4 weeks), and 18 patients (14%) did not improved. CSF returned to normal in 44 patients (34.4%), the median time 1 week (1 week, 2.75 weeks), improved in 45 patients (35.2%), the median time 2 weeks (2 weeks, 4 weeks), 25 patients(19.5%) not improved, and 14 patients (10.9%)did not check again.46 patients (35.9%) with CSF ink staining turned negative, and the median time was 16 weeks (7 weeks, 30 weeks), as shown in Table 1. There were 19 patients complete response (14.8%), 82 patients partial response (64.1%), 16 patients invalid response (12.5%), and 11 patients death (8.6%), as shown in Fig. 2. 101 patients (78.9%) were effectively treated, while 27 patients (21.1%) were not.

Table 1
Number and time of transition of AIDS patient with CM in the study cohort

Outcome		Number of cases (persons)	Time (weeks)
Symptoms	Disappeared	33(25.8%)	2(1.5, 3)
	Improved	77(60.2%)	3(2, 4)
	Not improved	18(14%)	-
CSF	Normal	44(34.4%)	1(1, 2.75)
	Improved	45(35.2%)	2(2, 4)
	No Improved	25(19.5%)	-
	No rechecked	14(10.9%)	-
CSF ink stains turn to negative		46(35.9%)	16(7, 30)

Note: CSF: cerebrospinal fluid; Median (Q1, Q3): median based on 25th and 75th percentiles.

3.2 Statistical analysis of data

The age of the ineffective group was higher than that of the effective group (P = 0.048, Table 2). Among the complication factors, the incidence of cerebral infarction in the group with ineffective clinical treatment was higher than that in the group with effective clinical treatment (P = 0.039, Table 2). Among the symptom and sign factors, the proportion of consciousness disorder in the group with ineffective clinical treatment was higher than that in the group with effective clinical treatment (P = 0.027, Table 2). There was no significant difference in CSF pressure, CSF routine and biochemistry, CSF ink staining, CSF and blood cryptococcus antigen and cryptococcus culture between the two groups. There were no significant differences in blood routine, infection markers, electrolytes, CD4 count and HIVRNA load between the two groups. The blood glucose of the ineffective group was higher than that of the effective group (P = 0.007). In terms of treatment timing/course and treatment regimen, there was no statistical difference between the effective and ineffective group in the clinical treatment. However, the duration of treatment in the induction period of the ineffective group was significantly shorter than that of the effective group (P < 0.001, Table 2).

Table 2
Clinical characteristics and data of AIDS patient with CM in the study cohort

Variables		Total (n = 128)	Effective cohort(n = 101)		Ineffective cohort (n = 27)		Statistic	*P*-value	
age		37.5(30.25, 46.75)	36(30, 44.5)		42.3 ± 13.5		-1.981	0.048	
Sex(cases)	Male	113(88.3%)	92(91.1%)		21(77.8%)		-1.903	0.057	
	Female	15(11.7)	9(8.9%)		6(22.2%)				
Complications (cases)	Tuberculous meningitis	14(10.9%)	9(8.9)	5(18.5%)			-1.415	0.157	
	Purulent meningitis	9(7%)	6(5.9%)	3(11.1%)			-0.930	0.352	
	Cryptococcal pneumonia	31(24.2%)	26(25.7%)	5(18.5%)			-0.775	0.438	
	Epilepsy	11(8.6%)	10(9.9%)	1(3.7%)			-1.017	0.309	
	Optic papillary edema	6(4.7%)	5(5%)	1(3.7%)			-0.271	0.786	
	Deafness	6(4.7)	6(5.9%)	0(0%)			-1.292	0.196	
	Hydrocephalus	3(2.3%)	2(2%)	1(3.7%)			-0.524	0.600	
	Cerebral hernia	4(3.1%)	2(2%)	2(7.4%)			-1.434	0.152	
	Cerebral infarction	8(6.3%)	4(4%)	4(14.8%)			-2.062	0.039	
Signs and symptoms (cases)	Fever	109(85.2%)		89(88.1%)	20(74.1%)			-1.816	0.069
	Sweat	29(22.7%)		24(23.8%)	5(18.5%)			-0.576	0.565
	Headache	119(93%)		93(92.1%)	26(96.3%)			-0.758	0.448
	Nausea and vomiting	95(74.2%)		76(75.2%)	19(70.4%)			-0.513	0.608
	Disturbance of consciousness	52(40.6%)		36(35.6%)	16(59.3%)			-2.211	0.027
	Eye disease	41(32%)		31(30.7%)	10(37%)			-0.625	0.532
	Cranial nerve injury	38(29.7%)		27(26.7%)	11(40.7%)			-1.410	0.159
	Neck resistance	82(64.1%)		65(64.4%)	17(63%)			-0.134	0.894
	Pathological signs	25(19.5%)		19(18.8)	6(22.2%)			-0.396	0.692
CSF pressure (mmH_2O)	< 180	25(19.5%)	23(22.8%)		2(7.4%)		-1.741	0.082	
	180–250	38(29.7%)	30(29.7%)		8(29.6%)				
	> 250	65(50.8%)	48(47.5%)		17(63%)				
CSF	WBC(cells/μl)	20(10, 59)	20(10, 61.5)		23(10, 50)		-0.138	0.891	
	TP(g/L)	40.4(30.8, 73.85)	38.6(30.5, 64.9)		50.3(30.9, 91)		-1.256	0.209	
	GLU(mmol/L)	2.45 ± 0.95	2.51 ± 0.89		2.24 ± 1.15		1.110	0.275	
	CL(mmol/L)	117.9 ± 6.38	118.47 ± 5.78		115.76 ± 8.02		1.647	0.109	
Positive (cases)	CSF Ink stain	105(82%)	84(83.2%)		21(77.8%)		-0.646	0.519	

Note: CSF: cerebrospinal fluid; WBC: white blood cell; TP: total protein; GLU: glucose; CL: chloride ion; NE% neutrophil%; LY% lymphocyte; HGB: hemoglobin; PLT: platelet; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; PCT: procalcitonin; K: potassium ion; Na: sodium ion; CD4: CD4 + T lymphocyte count; ART: antiretroviral therapy; AmB ± 5FC: amphotericin B ± 5-fluorocytosine; FLU ± 5FC: fluconazole ± 5-fluorocytosine; Median (Q1, Q3): median based on 25th and 75th percentiles.

Variables		Total (n = 128)	Effective cohort(n = 101)	Ineffective cohort (n = 27)	Statistic	*P*-value
	CSF Cryptococcus antigen	128(100%)	101(100%)	27(100%)	0.000	1.000
	CSF Cryptococcus culture	75(58.6%)	59(58.4%)	16(59.3%)	-0.079	0.937
	Blood Cryptococcus antigen	125(97.7%)	99(98%)	26(96.3%)	-0.524	0.600
	Blood Cryptococcus culture	67(52.3%)	54(53.5%)	13(48.1%)	-0.489	0.625
WBC(× 10^9/L)		4.97(3.37, 6.59)	4.94(3.19, 6.82)	5.57 ± 2.04	-0.873	0.383
NE%(%)		78.26(66.64, 83.26)	78.11(65.8, 82.58)	76.63 ± 13.56	-1.171	0.242
LY%(%)		12.97(7.92, 20.15)	12.92(7.97, 20.85)	14.89 ± 11.1	-0.447	0.655
HGB(g/L)		120.04 ± 22.59	118.76 ± 22.47	124.80 ± 22.84	-1.237	0.218
PLT(× 10^9/L)		175.5(128.5, 226.25)	176(117.5, 225.5)	166.50 ± 68.80	-0.517	0.605
ESR(mm/h)		41(21.5, 66)	46.17 ± 27.77	27(13, 68)	-1.481	0.139
CRP(mg/L)		13.05(4.58, 38.88)	14.7(5.46, 47.6)	7.5(3.6, 31)	-1.273	0.203
PCT(ng/ml)		0.05(0.05, 0.19)	0.06(0.05, 0.21)	0.05(0.05, 0.16)	-0.489	0.625
K(mmol/L)		3.58 ± 0.53	3.62 ± 0.53	3.43 ± 0.55	1.613	0.109
Na(mmol/L)		131.98 ± 5.51	132.09 ± 5.28	131.59 ± 6.38	0.417	0.677
Cl(mmol/L)		97.23 ± 5.54	97.42 ± 5.26	96.51 ± 6.54	0.756	0.451
GLU(mmol/L)		6.33(5.67, 7.46)	6.11(5.54, 7.04)	6.91(6.23, 8.1)	-2.695	0.007
CD4(cells/μl)		22.5(9.25, 47)	21(9, 46)	26(10, 55)	-0.973	0.331
HIV RNA(copies/ml)		68466.5(18675.5, 186018.5)	84218(14286, 182126)	31659(19412, 190202)	-1.072	0.284
Start/Unstart ART(cases)		32/96	25/76	7/20	0.016	0.901
Treatment timing/Course (weeks)		4(3, 8)	4(2, 8)	4(3, 9)	-0.672	0.502
therapeutic schedule (cases)	AmB ± 5FC	8(6.3%)	7(6.9%)	1(3.7%)	-1.825	0.068
	FLU ± 5FC	57(44.5%)	47(46.5%)	10(37%)		
	Voriconazole	4(3.1%)	4(4.0%)	0(0%)		
	Mixed regimens	39(30.5%)	31(30.7%)	8(29.6%)		
	Non-standard treatment	20(15.6%)	12(11.9%)	8(29.6%)		
Induction course (weeks)		5(3, 10)	7(4, 10)	2(1, 5)	-4.398	< 0.001

Note: CSF: cerebrospinal fluid; WBC: white blood cell; TP: total protein; GLU: glucose; CL: chloride ion; NE% neutrophil%; LY% lymphocyte; HGB: hemoglobin; PLT: platelet; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; PCT: procalcitonin; K: potassium ion; Na: sodium ion; CD4: CD4 + T lymphocyte count; ART: antiretroviral therapy; AmB ± 5FC: amphotericin B ± 5-fluorocytosine; FLU ± 5FC: fluconazole ± 5-fluorocytosine; Median (Q1, Q3): median based on 25th and 75th percentiles.

The results of multivariate Logistic regression analysis showed that the occurrence of cerebral hernia and disturbance of consciousness were risk factors for the prognosis of AIDS patients with CM. The occurrence of cerebral hernia increased the risk of poor prognosis of AIDS patients with CM by 405 times, and the occurrence of disturbance of consciousness increased the risk of poor prognosis by 4.4 times. The duration of treatment in the induction period was a protective factor for the prognosis of patients with AIDS complicated with CM. For each week of treatment in the induction period, the risk of poor prognosis was reduced by 0.683 times, and the effective outcome of clinical treatment was increased by 1.5 times. See Table 3 for details.

Table 3
Logistic regression analysis of prognostic factors of AIDS patients with CM

	B	S.E.	Wald	df	*P*-value	*OR*	95% CI of OR	
Cerebral hernia	6.003	2.144	7.838	1	0.005	404.617	6.052	27050.598
Disturbance of consciousness	1.476	0.533	7.661	1	0.006	4.376	1.539	12.444
Induction period treatment time	-0.381	0.102	14.052	1	< 0.001	0.683	0.560	0.834
Constant	-7.639	2.095	13.300	1	< 0.001	< 0.001		

Note: CI: Confidence Interval.

3.3 Prognostic analysis of shunt decompression therapy

The median time to shunt decompression was 7 weeks (5 weeks, 10 weeks). Six patients with shunt decompression completely responded, 17 partially responded, and 1 died. The clinically effective rate was 95.8%. 13 patients without shunt treatment completely responded, 65 patients responded partially, 16 patients failed, 10 patients died, and the clinical response rate was 75%. The independent sample nonparametric testfor the outcome of patients with shunt decompression and patients without shunt therapy was statistically different (Firgure 3, p = 0.016), and the prognosis of patients with shunt decompression was better than that of patients without shunt therapy.

In this study, 24 cases of shunt decompression treatment were included, including 5 cases of ventriculoperitoneal shunts (VP) (1 case underwent lumboperitoneal shunts again due to catheter blockage) and 19 cases of lumboperitoneal shunts (LP) (1 case underwent extubation and recatheterization due to infection, and 1 case was extubation due to catheter blockage). The start median time of shunt decompression therapy was 7 weeks (5 weeks, 10 weeks). There were 6 complete responses, 17 partial responses and 1 death in the patients treated with shunt decompression, with the clinical effective ratio of 95.8%. There were 13 cases of complete response, 65 cases of partial response, 16 cases of no response, 10 cases of death, and the clinical effective rate was 75%. Independent sample non-parametric test was performed between patients receiving shunt decompression treatment and those without shunt treatment, P = 0.016, showing a statistical difference. The prognosis of patients receiving shunt decompression treatment was better than that of patients without shunt treatment. (Fig. 3)

4. Discussion

The mortality of AIDS patients with CM in different income countries ranges from 10 to 43% [7]. Research results showed that the 2-week mortality rate of AIDS patients with CM was 17%, the 10-week mortality rate was 34%, and the overall 1-year mortality rate was 41% [8]. Even in developed countries, with the best antifungal and ART regimen, the mortality of HIV-associated CM within 10 weeks is still 10–25% [9]. The increase of intracranial pressure is positively correlated with the incidence and mortality of CM, and intracranial pressure increases with the increase of cerebrospinal fluid fungal load [3]. The timely and effective control of intracranial hypertension is one of the most critical factors in determining the outcome of CM, which can gain time for the success of antifungal therapy and reduce the early mortality of CM [10]. Comprehensive treatment of anti-cryptococcus, intracranial pressure management and ART are the key to reduce the mortality of patients with AIDS complicated with CM [11, 12].

The median duration of hospitalization in this study was 20 days (7 days, 41 days). With discharge as the observation endpoint, 11 patients died(8.6%), and 27 patients were ineffective in clinical treatment(21.1%). The mortality rate was similar to the literature report and low. In the study, the anti-cryptococcus treatment in induction period of the patients mainly included FLU ± 5-FC (44.5%) and successively FLU ± 5-FC, AmB ± 5-FC (30.5%), and AmB ± 5-FC (6.3%). Most of the patients choosed the FLU (800–1200 mg / d) ± 5-FC (100 mg / kg.d), mainly considering the obvious side effects of AmB and the high price of liposomal AmB. In terms of treatment timing/course of disease and treatment regimen, there was no statistical difference between the effective and ineffective group in the clinical treatment. Meta-analysis results showed that the AmB ± 5-FC regimen for AIDS patients complicated with CM may be better than other regimens, and FLU ± 5- FC may be an alternative without AmB[13]. A 10-year data-control analysis of the Affiliated Hospital of Sun Yat-sen University showed that FLU ± 5- FC

and AmB ± 5-FC in the treatment of CM were no statistically significant difference in CSF pressure, CSF cryptococcal number, CSF protein, CSF WBC and disease outcome [14]. The results of Molloy SF et al. showed that the induction period treatment regimens of 2-week FLU(1200 mg/d) + 5FC(100 mg/kg.d), 1-week AmB(1 mg/kg.d) and 2-week AmB(1 mg/kg.d) had similar mortality rates at 2 weeks and 10 weeks for AIDS patients with CM [15].In the United States, WHO and Chinese guidelines and expert consensus on the diagnosis and treatment of cryptococcal meningitis [6, 16, 17], different duration of induction period treatment, no matter not less than 2 weeks, or 4 weeks, or even 10–12 weeks, were all ended by CSF cryptococcus culture turn negative, followed by consolidation or maintenance treatment. The results of this study showed that the duration of induction period treatment in the ineffective group was significantly shorter than that in the effective group ($P < 0.001$), highlighting the importance of adequate time of induction period treatment in the guidelines and expert consensus.

The univariate analysis of the data in this study showed that the age and blood glucose of the clinically ineffective group were higher than those of the effective group, and the incidence of cerebral infarction and disturbance of consciousness was higher than that of the effective group. A 10-week follow-up study in Thailand, Uganda, South Africa and other countries showed that age over 50, changes in mental state, high fungal burden of CSF, removal rate of cryptococcus, and peripheral blood WBC > 10×10^9/L were independently correlated with early mortality of patients with AIDS complicated with CM [18]. The mechanism of cerebral infarction caused by CM may be related to extensive fibrosis of the subarachnoid space caused by cryptococcus, mechanically compress the small veins, and increased blood flow resistance [19].However, the correlation between the level of blood glucose, the occurrence of cerebral infarction and the poor prognosis of AIDS complicated with CM has not been reported at home and abroad. Considering that the single factor analysis reflects the difference between groups, it cannot reflect the causal relationship with the prognosis, so multivariate Logistic regression analysis was further conducted on the research data.

Next we found that the occurrence of cerebral hernia and disturbance of consciousness were risk factors for the prognosis of AIDS patients with CM, and the duration of induction therapy was a protective factor for the prognosis of AIDS patients with CM. The increase of intracranial pressure is positively correlated with the morbidity and mortality of CM [3]. Increased intracranial pressure is a prerequisite for the formation of cerebral hernia, which occur when intracranial pressure is unevenly distributed to a certain extent. Cerebral hernia itself has a very poor prognosis, high mortality and disability rate. Disturbance of consciousness is an independent risk factor for death in CM patients [4]. Lofgren et al. proposed that changesin mental state of CM patients lead to poor prognosis, and the change in mental state may be more related to the host immune response than the burden of cryptococcus [20]. The conclusion of this study that the occurrence of cerebral hernia and disturbance of consciousness are risk factors for the prognostic of AIDS patients with CM, which is consistent with many domestic and foreign research reports. However, the duration of treatment in the induction period is a protective factor for the prognosis of AIDS patients with CM, which is rarely reported at home and abroad. Considering the difficulty of CM treatment, the high fatality rate, the long course of disease, and the clearance rate of CSF cryptococcus is an independent risk factor for the mortality of CM in the early stage, andthe end ofthe induction period treatment is based on the CSF cryptococcus culture negative conversion, combined with the results of this study, anticryptococcal therapy with high efficiency and sufficient treatment time during induction period is especially critical for improving prognosis.

Another important result of this study is that the prognosis of patients receiving shunt decompression treatment is better than that of patients without shunt treatment. Despite severe immunodeficiency and persistent CNS cryptococcus infection, AIDS and CM patients with increased intracranial pressure have indication for LP and/or VP shunts[21]. Shunt surgery is usually a sustainable way to relieve the symptoms associated with increased intracranial pressure[22]. Baddley and others came to the same conclusion that shunt surgery may be earlier and more aggressive, and it may improve the prognosis associated with increased intracranial pressure in CM [23].

This study is a clinical retrospective study. Due to excessive loss of follow-up data, the analysis results of influencing factors of medium and long-term prognosis in patients with AIDS complicated with CM cannot be obtained, and the collected ART data cannot be evaluated. Due to the subjective choice of treatment options during the induction period of the previous case, the study subjects have biased in the distribution of treatment options, which affected the reliability of the conclusions obtained in terms of treatment timing/course of disease and treatment options. The above are the directions for further improvement in future research.

5. Conclusions

Cerebral hernia and disturbance of consciousness are risk factors for prognosis of AIDS patients with CM, and duration of induction therapy is a protective factor for prognosis. Anticryptococcal therapy with high efficiency and sufficient treatment time during induction period is especially critical for improving prognosis. Shunt decompression therapy may improve the prognosis of patients with AIDS complicated with CM.

Abbreviations

5-FC
5-fluorocytosine
AIDS
Acquired Immunodeficiency Syndrome
AmB
amphotericin B
ART
antiretroviral therapy
CM
cryptococcal meningitis
CNS
central nervous system
CSF
cerebrospinal fluid
FLU
fluconazole
HIV
Human Immunodeficiency Virus
LP
lumboperitoneal shunts
OI
opportunistic infection
VP
ventriculoperitoneal shunts
WB
Western blot test

Declarations

Ethics approval and consent to participate

This retrospective study was carried out in Beijing Ditan Hospital, Capital Medical University, and the study protocol was approved by the research ethics committee of hospital, which complied with principles of Declaration of Helsinki.

Consent for publication

All of clinical and laboratory data were used anonymously. Consent for publication is not applicable.

Availability of data and materials

The data used to support the findings of this study are available from the corresponding author upon request.

Competing interests

All authors declared that there are no conflicts of interest.

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Authors' contributions

Liang Wu contributed to this study and is the first author. The corresponding author is Professor Hongxin Zhao. All of the authors participated in the study.

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Figures

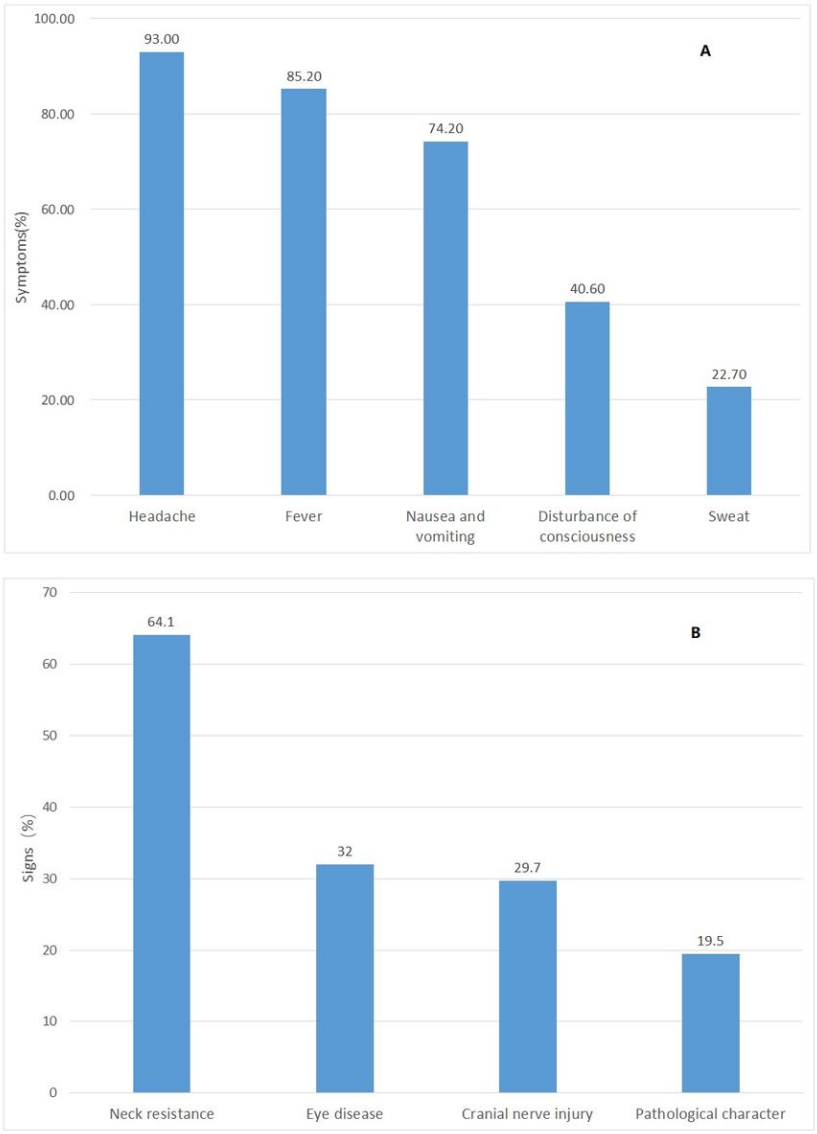

Figure 1

Occurrence rate of symptoms and signs of AIDS patient with CM.

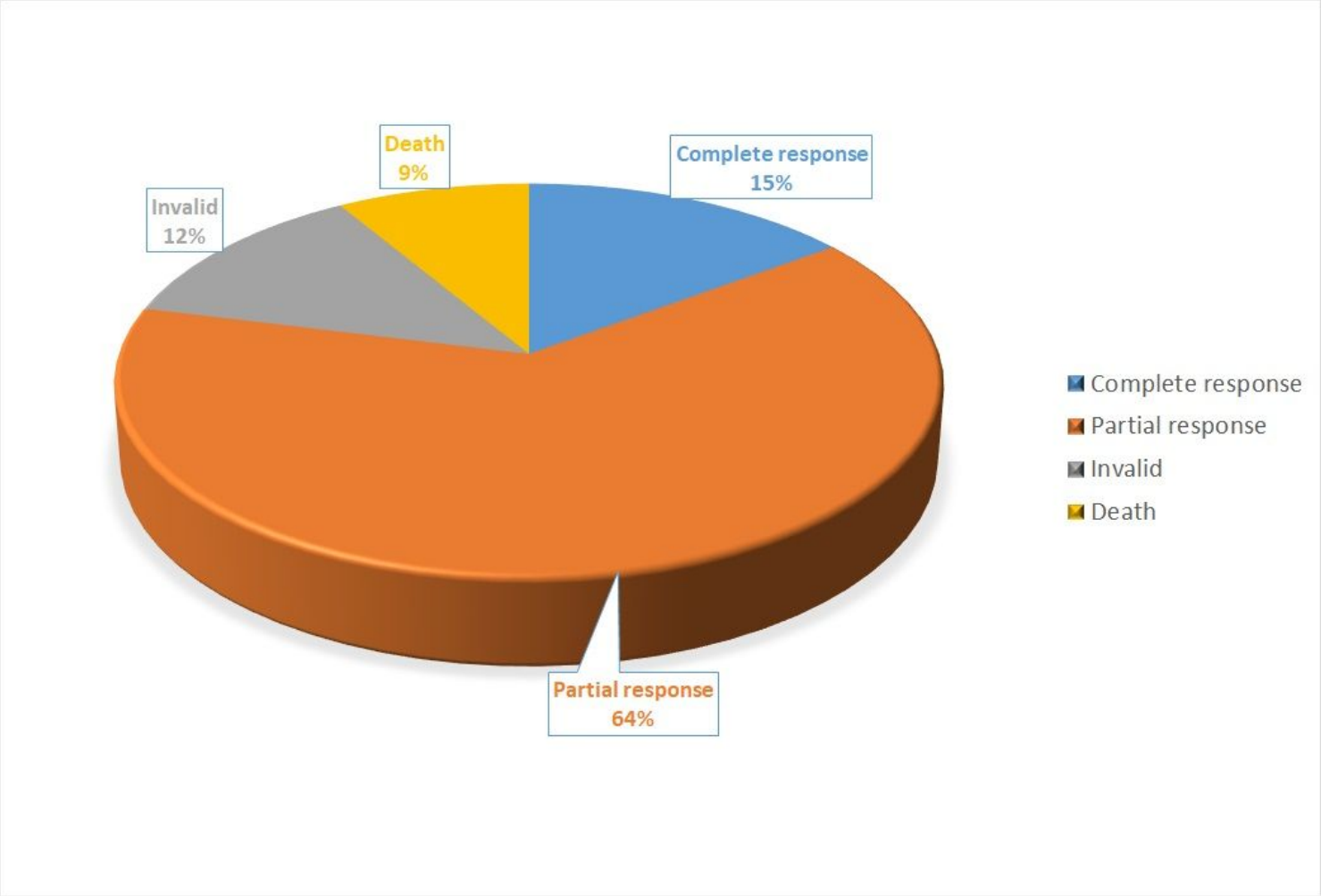

Figure 2

Schematic diagram of outcome of AIDS patient with CM in the study cohort.

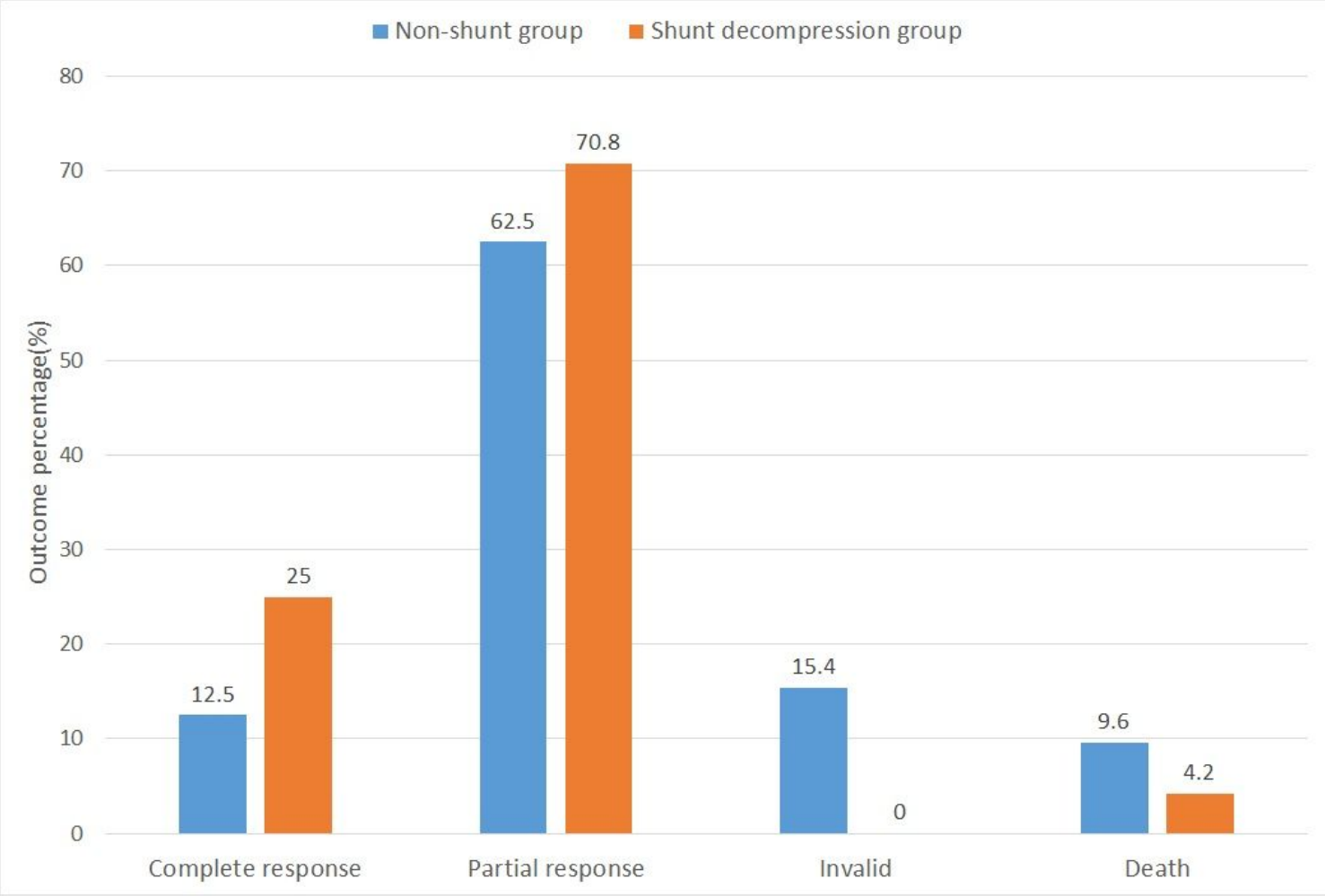

Figure 3

Outcome of AIDS patient with CM treated with shunt decompression/non-shunt therapy.