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Efficacy of Ventriculoperitoneal Shunt for Postoperative Central Nervous System Infection Complicated with Hydrocephalus

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Abstract

Objective Our aim was to assess the efficacy of ventriculoperitoneal shunt (VPS) for treating postoperative central nervous system infection (PCNSI) complicated with hydrocephalus and to identify factors associated with treatment failure.

Materials and Methods We conducted a retrospective analysis of PCNSI patients with hydrocephalus treated by VPS at the Department of Neurosurgery, the First Affiliated Hospital, College of Medicine, Zhejiang University, between December 2012 and January 2020. Functional recovery was evaluated during follow-up using the Glasgow Outcome Scale.

Results A total of 29 patients (21 males, 8 females) were enrolled in the study (mean age: 56.4 ± 12.0 years, range: 18.0–77.0 years). Seventeen patients were treated successfully by VPS (58.6%). Among the 11 patients with shunt complications (37.9%), 8 (27.6%) presented with fever, 3 (10.3%) with shunt infection, and 3 (10.3%) with shunt obstruction. Univariate analysis identified low Glasgow Coma Scale (GCS) score (3–8) at the time of VPS and post-treatment fever as predictive of shunt failure.

Conclusion VPS was effective for treating PCNSI complicated with hydrocephalus. However, patients with low GCS score at the time of VPS or fever post-treatment were at greater risk of shunt failure and poor outcome.

Keywords
- ventriculoperitoneal shunt
- postoperative central nervous system infection
- hydrocephalus

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Introduction

Postoperative central nervous system infection (PCNSI) is a serious complication of neurosurgery. While large-scale studies have reported incidences of approximately 1% or lower, infection rates may be increased substantially by immunosuppression and longer surgical duration among other factors.[1–4] Common sequelae of PCNSIs include meningitis/ventriculitis, epidural abscess, subdural empyema, and brain abscess,[3] and mortality in such cases is as high as 22 to 36%. Hydrocephalus is also a common complication of PCNSI, although reported incidence varies markedly across studies (11.6–60%).[5–8]

The diagnosis of hydrocephalus can be difficult in patients with inflammation associated with PCNSI, and delayed diagnosis is associated with poor prognosis, including residual neurological sequelae and increased mortality.[9,10] At present, ventriculoperitoneal shunt (VPS) placement is the primary treatment for hydrocephalus.[11] However, there are few reports on VPS for the treatment and management of PCNSI complicated with hydrocephalus. Therefore, we retrospectively evaluated the efficacy of VPS for PCNSI complicated with hydrocephalus and examined potential clinicodemographic factors predictive of shunt failure.

Materials and Methods

We retrospectively analyzed the medical records of 29 patients with PCNSI complicated by hydrocephalus and receiving VPS at the Department of Neurosurgery, First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China, between December 2012 and January 2020.

Inclusion and Exclusion Criteria

Study inclusion criteria were PCNSI complicated with hydrocephalus and VPS as the primary treatment. Exclusion criteria were a history of intracranial infection (including meningitis/ventriculitis, epidural abscess, subdural empyema, and brain abscess) and/or hydrocephalus prior to primary neurosurgical operation, history of intracranial surgery (including shunt surgery), and history of intracranial pathologies such as epidural hematoma, parenchymal hemorrhage, intraventricular hemorrhage, or ischemic insult.

Definitions

PCNSI was diagnosed by the presence of meningitis/ventriculitis, epidural abscess, subdural empyema, and/or brain abscess according to the criteria of the Centers for Disease Control and Prevention (CDC) with minor modifications.[3,12–14] According to the CDC, a confirmed case must meet at least one of the following criteria: (1) pathogens cultured from patient brain tissue, dura, and/or cerebrospinal fluid (CSF) samples; (2) evidence of intracranial infection on cranial computed tomography (CT), magnetic resonance imaging (MRI), or histopathological examination; (3) typical CSF findings of CNS infection such as glucose concentration less than 1.9 mmol/L, CSF glucose to blood glucose concentration ratio less than 0.23, protein level more than 2.2 g/L, white cell count more than 2,000 cells/μL; (4) at least two of headache, dizziness, fever ($>$ 38°C), stiff neck, irritability, and altered level of consciousness without other identifiable cause; (5) antibiotic treatment prescribed by the attending clinician.

Hydrocephalus was diagnosed by a dilated ventricular temporal horn without obvious brain atrophy and/or an Evan's ratio more than 0.3 on cranial imaging (CT or MRI). The Evan's ratio was calculated as the ratio of the bilateral frontal horn width to the maximum biparietal diameter.[15] The opening CSF pressure was measured from lumbar punctures at the time of infection.

A high Glasgow Coma Scale (GCS) score of 9 to 15 was considered good consciousness, while a low score of 3 to 8 was considered poor consciousness. For statistical analysis, intracranial pressure was divided into two categories according to the upper limit in normal adults[16]: those with a very high opening pressure ($>$ 200 mmH_2O) and those with a normal or moderately high pressure ($\leq$ 200 mmH_2O).

Antibiotic and Surgical Management

In all patients with suspected PCNSI, a sample of CSF was collected through lumbar puncture or lumbar drainage for examination and culture. All patients were treated with empirical antibiotics based on our clinical experience and previous published reports. Once the antibiogram for antimicrobial susceptibility was available, drug and dose were adjusted accordingly. In this cohort, the intravenous antibiotics administered were as follows: meropenem 0.5 to 1 g three times daily, linezolid 600 mg twice daily, tigecycline 50 to 100 mg twice daily, vancomycin 1 g twice daily, polymyxin B 500,000 to 1,000,000 IU twice daily, cefoperazone/sulbactam 2 g three times daily, amikacin 400 mg once daily, biapenem 300 mg three times daily, piperacillin/tazobactam 4.5 g three times daily, sulbactam 1 g three times daily, cefepime 2 g twice daily, ceftazidime 2 g three times daily, levofloxacin 500 mg once daily, and fluconazole 200 to 400 mg once daily. However, antibiotic dose and type were adjusted if abnormalities in liver and kidney function arose. Some patients also received intraventricular antibiotic injection. The decision to initiate intraventricular antimicrobial therapy was made by the neurosurgeon and the infectious diseases consultant.

The main indication for VPS was further deterioration of neurological status or worsening mental acuity due to hydrocephalus. Patients developing hydrocephalus during active PCNSI received external ventricular drainage (EVD), lumbar drainage, Ommaya reservoir implantation, or regular lumbar puncture. If PCNSI was successfully cured, VPS was then used to treat hydrocephalus at the neurosurgeon's discretion. According to our clinical experience, CSF samples were tested at least twice every 2 to 3 days and VPS performed after at least two negative tests if temperature remained below 38°C during this monitoring period.

Outcome and Follow-Up

Therapeutic outcomes were determined using the Glasgow Outcome Scale (GOS) score as follows[17]: GOS 1: death; GOS

2: persistent vegetative state and/or minimal responsive state; GOS 3: conscious but disabled; GOS 4: disabled but independent; GOS 5: good recovery, resumption of normal life, there may be minor neurological and psychological deficits and changes in GCS before and after shunting at 6 months after placement of the VPS. Treatment success was defined as GOS score equal to 3 or more and improved (numerically higher) or unchanged GCS score. Treatment failure was defined as GOS score less than 3 and reduced GCS score, and/or by serious complications that required shunt adjustment, shunt replacement (the VPS is removed and replaced by a new device), or shunt removal without replacement. The follow-up time was at least 6 months after completion of VPS. Follow-up information was obtained by reviewing records of hospital admissions and outpatient clinic visits. This study was approved by the institutional ethics committee. The requirement for informed consent from patients was waived because the datasets were anonymized. All methods were performed in accordance with the relevant guidelines and regulations.

Data Collection

Demographic, clinical, radiological, and laboratory data as well as other relevant information for analysis were collected from standardized case reports and entered into a database. The following information were included in the analysis: sex, age, primary diagnosis, surgical history prior to PCNSI, pathogen, laboratory findings after infection, clinical characteristics at admission and at the time of VPS, main intravenous and intrathecal antibiotics used, CSF opening pressure, need for surgery after infection (yes/no) and procedure, complications after VPS, time interval from last operation to PCNSI (days), time interval from last negative CSF culture to VPS (days), hospitalization time (days), and 6-month post-VPS GCS and GOS scores.

Statistical Analyses

Continuous data are presented as mean ± standard deviation and categorical data as frequency. Univariate analysis was used to identify predictors of treatment failure. A p-value less than 0.05 (two-tailed) was considered statistically significant for all tests. SPSS software (version 16.0) was used for statistical analysis.

Results

Baseline Clinical Characteristics

A total of 29 patients (21 males and eight females; mean age 56.4 ± 12.0 years, range: 18.0–77.0 years) treated by VPS for PCNSI complicated with hydrocephalus were enrolled according to inclusion and exclusion criteria. The mean duration of hospitalization was 87.9 ± 52.7 days (range: 33.0–288.0 days). Primary diagnosis, surgical history before PCNSI, clinical characteristics at admission, operations required after PCNSI, type of hydrocephalus, and clinical characteristics before VPS are summarized in ►**Table 1**.

The CSF culture of 21 patients (72.4%) was positive, including 14 patients (48.3%) with single microbial infection and seven (24.1%) with mixed microbial infection. In total, 27 infectious microorganisms were identified, including 15 (55.6%) gram-positive bacteria, 11 (40.7%) gram-negative bacteria, and one (3.7%) fungus. Most gram-positive bacteria were staphylococci (12 cases, 44.4%), while most gram-negative micoorganisms were Bacilli (nine cases, 33.3%), and the one case (3.7%) of fungal infection was from *Candida parapsilosis*. The mean duration from the last CNS operation to confirmed PCNSI was 20.9 ± 20.2 days (range: 3.0–90.0 days). All patients received intravenous antibiotics and two patients also received intraventricular/intrathecal antibiotics, one treated with vancomycin 20 mg once daily for *Enterococcus faecalis* and *Staphylococcus hominis* infection (through Ommaya reservoir, duration 5 days), and the other with polymyxin B 100,000 IU every 12 hours for *Acinetobacter baumannii* infection (through lumbar drainage, duration 28 days). The mean duration of intravenous antibiotic treatment was 33.1 ± 10.8 days (range: 11.0–51.0 days).

Outcome and Complications of VPS: Analysis of Risk Factors for Failure

Seventeen patients (58.6%, 12 males and five females) were treated successfully by VPS, while 12 patients (41.4%, nine males and three females) were deemed treatment failures. Mean patient age did not differ significantly between treatment successes and failures (58.3 ± 7.6 years vs. 53.8 ± 16.4 years, $p = 0.33$). Among the 21 patients with positive CSF culture, the mean delay from the last negative CSF culture to VPS was 62.3 ± 52.3 days (range: 7.0–190.0 days). Among the treatment failure patients, nine (31.1%) were in a vegetative state, one died (mortality rate of 3.4%), and five (17.2%) demonstrated a GCS score decrease (deteriorated status) during follow-up.

The GCS score at the time of VPS was rated as good (9–15) in 14 patients (48.3%) and poor (3–8) in 15 (51.7%) patients. The majority of patients in the good consciousness group were deemed treatment successes (11 [78.6%] vs. 3 [21.4%] failures). In the poor consciousness group, six (40%) patients were treatment successes and nine (60%) were treatment failures. The GCS score at the time of VPS was significantly correlated with the 6-month outcome as evaluated by the GOS ($p = 0.035$). Therefore, the GCS 9 to 15 score subgroup demonstrated better outcome than the GCS less than or equal to 8 score subgroup.

Complications occurred in 11 patients (37.9%), including 8 (27.6%) cases of fever, 3 (10.3%) of shunt infection, and 3 (10.3%) of shunt obstruction during follow-up. Among patients with fever, six (75.0%) were treatment failures and only two (25.0%) were treatment successes. Fever after VPS was significantly correlated with the 6-month outcome ($p = 0.038$). Among patients with shunt infection, two were treatment failures, of which one received shunt removal without replacement. Of the three patients with shunt obstruction, two received shunt adjustment and another shunt replacement. Details of the outcomes and complications of VPS are presented in ►**Table 2**. Other variables that were not significantly correlated with treatment failure are summarized in ►**Table 3**.

Table 1 Clinical characteristics of patients

Variables	*n* (%)
Total patients	29
Gender	
Male	21 (72.4)
Female	8 (27.6)
Age, mean ± SD, years	56.4 ± 12.0 (18.0–77.0)
Primary diagnosis	
Traumatic brain injury	16 (55.2)
Intracerebral hemorrhage	11 (37.9)
Brain tumor	1 (3.4)
Intracranial artery occlusion	1 (3.4)
Operation of patients before PCNSI	
Hematoma evacuation	23 (79.3)
Decompressive craniectomy	21 (72.4)
External ventricular drainage	11 (37.9)
Intracranial pressure monitoring	7 (24.1)
Cranioplasty	3 (10.3)
Lumbar drainage	2 (6.9)
Ommaya implantation	1 (3.4)
Intracranial artery stent implantation	1 (3.4)
Tumor resection	1 (3.4)
Clinical characteristics at admission	
GCS	
9–15	11 (37.9)
3–8	18 (62.1)
Temperature > 38°C	28 (96.6)
Neck stiffness	13 (44.8)
Change of consciousness	8 (27.6)
Motor weakness	3 (10.3)
CSF opening pressure	
≤ 200	19 (65.5)
> 200	10 (34.5)
Laboratory findings	
CSF culture positive	21 (72.4)
Single infection	14 (48.3)
Mixed infection	7 (24.1)
CSF culture negative	8 (27.6)
CSF WBC count, cells/μL (median, IQR)	800.0 (135.0–3,150.0)
CSF protein, g/L (median, IQR)	1.75 (0.98–3.27)
CSF glucose, mmol/L (mean ± SD)	2.8 ± 1.9
CSF: blood glucose ratio (mean ± SD)	0.32 ± 0.22
Operation of patients after PCNSI	
Lumbar puncture	29 (100.0)
Lumbar drainage	20 (69.0)
External ventricular drainage	10 (34.5)
Intracranial abscess removal	2 (6.9)
Ommaya implantation	1 (3.4)
Types of hydrocephalus	
Communicating hydrocephalus	25 (86.2)
Obstructive hydrocephalus	4 (13.8)
Clinical characteristics at the time of VPS	
Neck stiffness	3 (10.3)
GCS	
9–15	14 (48.3)
3–8	15 (51.7)

Abbreviations: CSF, cerebrospinal fluid; GCS, Glasgow Coma Scale; IQR, interquartile range; PCNSI, postoperative central nervous system infection; SD, standard deviation; VPS, ventriculoperitoneal shunt; WBC, white blood cells.

Table 2 Outcomes and complications after VPS during follow-up

Outcomes	*n* (%)
Treatment success	17 (58.6)
Treatment failure	12 (41.4)
GOS	
1	1 (3.4)
2	9 (31.1)
3	16 (55.2)
4	2 (6.9)
5	1 (3.4)
GCS changes	
Improvement	10 (34.5)
Unchanged	14 (48.3)
Deterioration	5 (17.2)
Complications	11 (37.9)
Fever	8 (27.6)
Shunt infection	3 (10.3)
Shunt obstruction	3 (10.3)
Poor wound healing	2 (6.9)
Epilepsy	2 (6.9)
Intracranial hemorrhage	1 (3.4)

Abbreviations: GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; VPS, ventriculoperitoneal shunt.
GOS 1: death; GOS 2: persistent vegetative state and/or minimal responsive state; GOS 3: conscious but disabled; GOS 4: disabled but independent; GOS 5: good recovery, resumption of normal life, there may be minor neurological and psychological deficits.

Table 3 Univariate risk factors for treatment failure in patient of VPS in patients with PCNSI complicated with hydrocephalus

Variables	Treatment success	Treatment failure	*p*-Value
Patients	17 (%)	12 (%)	
Gender			NS
Male	12 (57.1)	9 (42.9)	
Female	5 (62.5)	3 (37.5)	
Age (mean ± SD, years)	58.3 ± 7.6	53.8 ± 16.4	NS
Underlying neurological condition			
Traumatic brain injury	10 (62.5)	6 (37.5)	NS
Intracerebral hemorrhage	6 (54.5)	5 (45.5)	NS
Brain tumor	1 (100.0)	0	__
Intracranial artery occlusion	0	1 (100.0)	__
Operation of the patient before infection			
Hematoma evacuation	14 (60.9)	9 (39.1)	NS
Decompressive craniectomy	14 (66.7)	7 (33.3)	NS
External ventricular drainage	4 (36.4)	7 (63.6)	NS
Intracranial pressure monitoring	2 (28.6)	5 (71.4)	NS
Cranioplasty	2 (66.7)	1 (33.3)	NS
Intracranial artery stent implantation	0	1 (100.0)	__
Ommaya implantation	1 (100.0)	0	__
Lumbar drainage	1 (50.0)	1 (50.0)	NS
Tumor resection	1 (100.0)	0	__
Time interval from last operation to infection (mean ± SD, days)	22.8 ± 22.4	18.2 ± 17.2	NS
Clinical characteristics at admission			
GCS			NS
9–15	6 (54.5)	5 (45.5)	
3–8	11 (61.1)	7 (38.9)	
Temperature > 38°C	16 (57.1)	12 (42.9)	__
Neck stiffness	8 (61.5)	5 (38.5)	NS
Change of consciousness	5 (62.5)	3 (37.5)	NS
Motor weakness	1 (33.3)	2 (66.7)	NS
CSF opening pressure			NS
≤ 200	10 (58.8)	7 (41.2)	
> 200	7 (58.3)	5 (41.7)	
Laboratory findings			
CSF culture positive	11 (52.4)	10 (47.6)	NS
CSF WBC count, cells/μL, mean ± SD	2,070.8 ± 2,822.1	2,113.2 ± 3,018.4	NS
CSF protein, g/L, mean ± SD	1.7 ± 1.0	5.4 ± 6.4	NS
CSF glucose, mmol/L, mean ± SD	2.4 ± 1.6	3.3 ± 2.3	NS
CSF: blood glucose ratio, mean ± SD	0.33 ± 0.26	0.30 ± 0.17	NS
Operation of the patient after infection			
Lumbar puncture	17 (58.6)	12 (41.4)	__
Lumbar drainage	14 (70.0)	6 (30.0)	NS
External ventricular drainage	5 (50.0)	5 (50.0)	NS
Ommaya implantation	1 (100.0)	0	__

Table 3 (*Continued*)

Variables	Treatment success	Treatment failure	*p*-Value
Intracranial abscess removal	2 (100.0)	0	—
Intraventricular	2 (100.0)	0	—
Hydrocephalus type			NS
Communicating hydrocephalus	15 (60.0)	10 (40.0)	
Obstructive hydrocephalus	2 (50.0)	2 (50.0)	
Clinical characteristics at the time of VPS			
Neck stiffness	2 (66.7)	1 (33.3)	NS
GCS			0.035
9–15	11 (78.6)	3 (21.4)	
3–8	6 (40.0)	9 (60.0)	
Complications after VPS			
Fever	2 (25.0)	6 (75.0)	0.038
Shunt infection	1 (33.3)	2 (66.7)	NS
Shunt obstruction	1 (33.3)	2 (66.7)	NS
Poor wound healing	2 (100.0)	0	—
Epilepsy	0	2 (100.0)	—
Intracranial hemorrhage	0	1 (100.0)	—
Hospitalization time, mean ± SD, days	78.9 ± 32.7	100.5 ± 72.3	NS

Abbreviations: CSF: cerebrospinal fluid; GCS, Glasgow Coma Scale; NS, not significant; SD, standard deviation; VPS, ventriculoperitoneal shunt.

Discussion

Hydrocephalus is one of the main causes of morbidity and mortality among patients with PCNSI.[9,18,19] Inflammation of the meninges or/and ventricles from PCNSI may cause hydrocephalus by impairing CSF circulation and absorption.[20] Temporary measures for the management of hydrocephalus include EVD, lumbar drainage, Ommaya reservoir implantation, and regular lumbar puncture,[21] while VPS is currently the most popular permanent treatment.[22] However, there are no widely recognized criteria to select PCNSI patients most likely to benefit from PVS placement in case of hydrocephalus, so we conducted this retrospective analysis of clinical differences between good and poor outcome groups.

The PCNSI must be cured before VPS placement. In our study, all patients were treated with intravenous antibiotics prior to VPS surgery, including with intraventricular/intrathecal antibiotics in two cases (neither of which experienced adverse effects). Eight of the 29 presumed PCNSI patients were negative according to multiple CSF cultures, but the CSF contained high levels of protein, elevated leucocyte counts, and low glucose indicative of ongoing CNS infection, and so were diagnosed with PCNSI. The specific intravenous antibiotic regimens for these eight patients were chosen according to our clinical experience and previous reports.[23] During these treatments, we used an external drainage system to clear 150 to 250 mL of CSF every 24 hours for hydrocephalus control and CSF renewal.

During follow-up, 17 patients were judged as treatment successes according to GOS score (58.6%), in accordance with the result of Liliang et al (63%),[24] while 12 were judged as treatment failures, including one fatality (3.4%), a rate lower than reported by Liliang et al (22.2%). The total incidence of VPS complications (37.9%) was also within the range of previous studies (17–38%), as were the incidences of shunt infection (10.3 vs. 5.6–12.9% in previous reports) and shunt obstruction (10.3 vs. 7.8–31.4%).[22,25–27] Factors demonstrated to influence the outcome of intracranial infection include low CSF glucose, high CSF leukocyte count, high CSF protein level, poor level of consciousness, and hydrocephalus[6,23]; however, to the best of our knowledge no study has examined the influence of hydrocephalus accompanying intracranial infection on outcome in a relatively large cohort with statistical analysis. Univariate analysis identified a significant association between poor consciousness (GCS 3–8) at the time of VPS and treatment failure after shunt placement. Most patients with poor consciousness had GOS scores less than 3 or showed no GCS improvement during follow-up, possibly because such patients had already developed irreversible brain tissue damage before VPS. Alternatively, it is possible that the follow-up time was insufficient to document slower but substantial recovery.

Fever after shunt was also significantly associated with treatment failure by univariate analysis. Six of the eight patients with fever demonstrated poor outcome at follow-up, of which two cases were due to shunt infection and the other four to infection of other organs or sepsis. We hypothesized that treatment failure after shunt surgery may have resulted from multiple organ failure due to incomplete control of infection.

This study has two main limitations. First, the retrospective design may have introduced selection bias. Further,

some results of CSF microbial culture were not included in the records. Second, the sample size was small, precluding detailed analysis of other potential factors influencing outcome.

Conclusion

In this study, we evaluated risk factors associated with VPS treatment failure in PCNSI patients complicated by hydrocephalus. Treatment success rate was 58.6%, and treatment failure was associated with a low GCS score at the time of VPS and fever after shunt implantation. Larger prospective multicenter studies are warranted to confirm these findings.

Authors' Contributions

X.F.Y. and H.W. designed research, performed research, analyzed data. F.M.C., L.W., K.L.X., and T.X.Z. collected data, analyzed the data, and drafted the manuscript. N.W., Z.Y.H., Q.Z., and X.S.Z. collected and analyzed the data. All authors checked and agreed on the final manuscript.

Ethical Approval

This study was approved by the ethics committees of the First Affiliated Hospital, Zhejiang University School of Medicine. The requirement for obtaining informed consent from patients was waived because the datasets were anonymous. All methods were performed in accordance with the relevant guidelines and regulations.

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Conflict of Interest

None declared.

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