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Outcomes of Tuberculous Meningitis Patients with Hydrocephalus with or without Cerebrospinal Fluid Diversion

Nabila Chantikarizky Hasanah,[1] Akhmad Imron,[2] Ahmad Rizal Ganiem[3]

[1]Faculty of Medicine Universitas Padjadjaran, Indonesia, [2]Department of Neurosurgery Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, [3]Department of Neurology, Faculty of Medicine Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

Abstract

Background: Hydrocephalus is a common complication in tuberculous meningitis patients and is a poor predictor with high mortality and morbidity rates. Therefore, early diagnosis, detection, and treatment of hydrocephalus are important. Cerebrospinal fluid diversion is the process used to drain accumulated fluid in the brain and spinal cord. This study aimed to explore the outcome of tuberculous meningitis patients with hydrocephalus who underwent cerebrospinal fluid diversion and who did not.

Methods: This was a retrospective cross-sectional descriptive study, including tuberculosis meningitis patients with hydrocephalus, admitted at the Department of Neurology Dr. Hasan Sadikin Bandung General Hospital during the period 2018. Functional outcomes were grouped based on the Glasgow Outcome Scale.

Results: Of the 55 patients, only 14 (25.5%) underwent cerebrospinal fluid diversion. The outcome of patients with cerebrospinal fluid diversion was 8 of 14 good, 1 of 14 poor, and 5 of 14 died. The outcome of patients without cerebrospinal fluid diversion was 13 of 41 good, 2 of 41 poor, and 26 of 41 died. Most tuberculous meningitis patients with hydrocephalus, with or without the cerebrospinal fluid diversion procedure were at an advanced stage with a high mortality rate.

Conclusion: The proportion of good functional outcomes in patients with cerebrospinal fluid diversion is higher than in patients without the cerebrospinal fluid diversion.

Keywords: Cerebrospinal fluid diversion, hydrocephalus, outcome, tuberculous meningitis

Introduction

Tuberculosis (TB) is a major cause of health problems and is one of the ten causes of death worldwide.[1] Of all TB cases, extrapulmonary TB accounts for 20–25%. Tuberculous meningitis infects the meninges lining of the brain and is the most severe form of extrapulmonary TB, which can cause disability and death.[2] Hydrocephalus is a complication often found in patients with tuberculous meningitis and is one of the poor predictors.[3] Hydrocephalus can be classified into communicating and non-communicating hydrocephalus.[4] In tuberculous meningitis, hydrocephalus occurs due to impaired cerebrospinal fluid (CSF) flow in the subarachnoid space caused by inflammatory infiltrates. Furthermore, CSF flow obstruction causes enlargement of the ventricular system of the brain and may be accompanied by increased intracranial pressure.[5]

The management of hydrocephalus in tuberculous meningitis patients varies, and until now, there are no specific universal guidelines regarding surgical management indications.[6] Treatment of hydrocephalus can be done with drugs or with operative measures as indicated. Non-communicating hydrocephalus is a life-threatening condition, so the use of drugs is considered ineffective and usually requires an operative procedure

Correspondence: Nabila Chantikarizky Hasanah, Faculty of Medicine Universitas Padjadjaran, Jalan Raya Bandung Sumedang Km. 21 Jatinangor, Sumedang Indonesia, E-mail: nabila.chantika@gmail.com

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in the form of CSF diversion, namely, shunt surgery such as ventriculoperitoneal shunt and ventriculoatrial shunt, external ventricular drain, and endoscopic third ventriculostomy.[4,7] The most common types of CSF diversion are ventriculoperitoneal (VP) shunt and external ventricular drain (EVD).

The high mortality and morbidity rates in tuberculous meningitis patients with hydrocephalus require proper diagnosis, early treatment, and hydrocephalus treatment.[3,4,8] Nevertheless, there is still diversity and uncertainty in the outcome of patients undergoing CSF diversion procedures until now.[4,6] Therefore, a descriptive study is needed to determine the outcome of tuberculous meningitis patients with hydrocephalus who underwent CSF diversion. This study aimed to explore the outcome of tuberculous meningitis patients with hydrocephalus who underwent CSF diversion and who did not.

Methods

The study was conducted with a cross-sectional retrospective descriptive method in tuberculous meningitis patients with hydrocephalus at the Department of Neurology Dr. Hasan Sadikin General Hospital Bandung admitted during 2018. A total sampling was conducted, with inclusion criteria being adults aged >18 years, diagnosed with tuberculous meningitis and with hydrocephalus as evidenced by brain imaging results. Data on patients who discontinued the treatment were excluded from the study. The research received approval from the Research Ethics Committee of Universitas Padjadjaran number 630/UN6.KEP/EC/2020 and a research permit according to the Research and Research and Ethics Committee of Dr Hasan Sadikin General Hospital.

Data on body temperature at admission in the hospital were noted. The severity of tuberculous meningitis was grouped into three levels according to the British Medical Research Council (BMRC) based on Glasgow Coma Scale (GCS) and the presence of neurologic deficits was defined as follows; grade 1 was defined as a GCS score of 15 without focal neurologic deficit, grade 2 as GCS 11–14 or GCS 15 with neurologic deficit, and grade 3 as GCS 10. Head imaging results confirming the diagnosis of hydrocephalus were retrieved by measuring ventricular enlargement using the Evans' ratio by comparing the length of maximum ventricular width and the maximum width of the calvaria bone with more than 0.3 considered as hydrocephalus. Indications of CSF diversion were based on the initial level of consciousness, and neurological status.[9]

Outcome data were grouped based on the Glasgow Outcome Scale (GOS) with the following interpretation: GOS value of 1 was designated as death; GOS value of 2 was for comatose patient; GOS value of 3 was for sopor or somnolent patient, or otherwise patient with the motoric strength 0 to 3, or there was a language disorder; GOS value of 4 was for patient in a composted state with a degree of motoric strength of 4; and GOS value of 5 in a patient in a composted state with a final degree of motor strength of 5 or having mild neurological sequelae. The GOS was assessed based on measurement just before discharge from the hospital. Furthermore, the outcome was grouped into good functional outcome, poor functional outcome, and death; GOS 1 would be death, GOS 2 and 3 would be classified as poor functional outcomes, and GOS 4 and 5 would be classified as good functional outcomes.

Results

In 2018, 146 patients were treated for tuberculous meningitis at Dr. Hasan Sadikin General Hospital, 65 (44.5%) of patients had hydrocephalus. Of the 65 tuberculous meningitis with hydrocephalus, only 55 patients (85%) met the inclusion criteria, and 10 (15%) were excluded for several reasons such as 4 (6%) were discharged at their request, 5 (8%) had an outcome that could not be assessed due to the patient switched treatments, and 1 (2%) was under the influence of medication. This study divided patients (n=55) into two criteria based on their management which were with CSF diversion (n=14; 25%) and without CSF diversion (n=41; 75%).

Characteristics of tuberculous meningitis patients with hydrocephalus are shown in Table 1. There was no difference in the proportions related to demographic characteristics of tuberculous meningitis patients and clinical symptoms that were only given drug therapy or with CSF diversion procedures (Table 1).

Table 2 shows an overview of the proportion of characteristics related to the management. The most common type of nosocomial infection in patients was hospital acquired pneumonia. All patients were given anti-tuberculosis drug therapy and dexamethasone. The most common cause of death was non-neurological causes in the form of nosocomial infections. In

patients with CSF diversion, VP shunt was the most common type of performed procedure (13 of 14).

In terms of the proportion of patients' outcome based on the severity of tuberculous meningitis and the GOS underwent CSF diversion action, it was found that 8 patients treated with CSF diversion had good outcomes: GOS 4 was 3, and GOS 5 was 5. A total of 5 patients died, and 1 patient had a poor outcome GOS 3 (Table 3).

Table 4 shows the proportion of patients' outcome based on the severity of tuberculous meningitis and the GOS underwent CSF diversion action, who were only given therapy in the form of drugs. Most of the patients died (n=26; 63%), and 2 (5%) had poor functional outcome. Only 13 (32%) had good functional outcome (Table 4).

Discussions

The proportion of hydrocephalus in tuberculous meningitis patients in this study is 44.5%, similar to a 6-year retrospective study conducted in Northern Taiwan with a percentage of 44.4%.[3] This study reveals no difference in the proportion related to demographic characteristics or clinical symptoms between patients who were given only drug therapy and those who underwent CSF diversion. The mean age of patients was 32 years (IQR 26–42). The majority of patients in this study were male, similar to a previous study in the Department of Neurology Dr. Hasan Sadikin General Hospital for the period January 2014–September 2016.[10]

Tuberculous meningitis is an infection that triggers the immune system and

Table 1 Characteristics of Tuberculous Meningitis Patients with Hydrocephalus with or without CSF Diversion admitted in Dr. Hasan Sadikin General Hospital in 2018

Characteristics	With CSF Diversion (n=14)	Without CSF Diversion (n=41)
	n	n (%)
Male	8	25 (61)
Age in years–median (IQR)	33 (24.25–44.25)	32 (27.5–49)
Chief complaint		
Altered sensorium	13	36 (88)
Headache	1	3 (7)
Seizures	0	2 (5)
Body temperature (°C)–median (IQR)	36.95 (36.5–37.1)	37.5 (37–37.8)
Level of consciousness		
Compos mentis (GCS 15)	1	3 (7)
Somnolent (GCS 12–14)	13	30 (73)
Sopor (GCS 8–11)	0	8 (20)
Coma (GCS 3–7)	0	0 (0)
Motoric level		
Normal	3	11 (27)
Hemiparesis/hemiplegia	8	19 (46)
Tetraparesis/tetraplegia	3	9 (22)
Paraparesis/paraplegia	0	2 (5)
Degree of tuberculous meningitis (MRC staging)		
Stage I	0	0 (0)
Stage II	12	31 (76)
Stage III	2	10 (24)
Anti-HIV positive *	0 of 12	5 of 34
Imaging (CT scan)		
Communicating hydrocephalus	11	32 (78)
Non-communicating hydrocephalus	3	9 (22)

Note: Information on HIV (human immunodeficiency virus) status was only available for 46 people, namely n=12 with CSF diversion and n=34 without CSF diversion

Table 2 Management of Tuberculous Meningitis Patients with Hydrocephalus with or without CSF Diversion, admitted in Dr. Hasan Sadikin General Hospital in 2018

Characteristics	With CSF Diversion (n=14)	Without CSF Diversion (n=41)
	n	n (%)
Length of inpatient staying days – median (IQR)	21.5 (11.5– 27.5)	5 (3 – 19.5)
Nosocomial infections		
Hospital acquired pneumonia	4	10 (24)
Catheter-associated urinary tract Infections/urosepsis	1	3 (7)
Others	0	1 (2)
Without infections	9	28 (68)
Drug administration		
Anti-tuberculosis drugs	14	41 (100)
Corticosteroids	14	41 (100)
Acetazolamide	2	15 (37)
Duration between the decision and the CSF diversion procedure		
< 1 day	10	N/A
> 1 day	4	N/A
CSF diversion types		
Ventriculoperitoneal (VP) shunt	13	N/A
External ventricular drain (EVD)	1	N/A
Length of stay for patients who died§ (days) – median (IQR)	12 (9 – 64)	3.5 (1.75 – 5)
Cause of death§		
Non-neurological causes	4	14 (54)
Neurological causes	1	12 (46)

Note: Information on the length of treatment for patients who died and the cause of death was n=5 in patients with CSF diversion and n=26 in patients without CSF diversion

releases cytokines that can increase body temperature.[11] In this study, there were variations in the patients' body temperature with a mean value of 37.3 °C (IQR 36.8 °C–37.8 °C). Decreased consciousness at the somnolent level is the most frequent clinical symptom that underlies the patient being admitted to the hospital and. is related to the severity of tuberculous meningitis and can be a marker of hydrocephalus.[4,12]

Hydrocephalus is a common complication of tuberculous meningitis. It is associated with poor outcome.[4,13] Hydrocephalus can cause an increase intracranial pressure, causing various clinical symptoms and requiring immediate action.[14] According to a previous research, communicating hydrocephalus types are more often found in cases of tuberculous meningitis than non-communicating types,[4] in line with the findings of our study. The management of hydrocephalus in tuberculous meningitis patients varies. In our study, patient management was carried out with medical therapy in drugs or CSF diversion measures such as VP shunt/EVD if indicated.

The outcome in tuberculous meningitis patients with hydrocephalus is related to several things. The presence of hemiparesis, paraparesis, and grade III of tuberculous meningitis may lead to a poor prognosis.[4] Our study found that a large number of patients had hemiparesis and paraparesis, 22% of patients had grade III MRC tuberculous meningitis. This percentage is similar to the findings of the proportion in a study in Malaysia, which stated that patients with grade III were 22.8%.[15] Furthermore, there is a relationship between the severity of tuberculous meningitis and poor outcome[3], as was also found in our study which showed that of the total patients with meningitis grade III, 92% of patients died.

The length of inpatient stay can also determine the outcome. Interestingly, there is an interplay between the length of stay of patients and the presence of nosocomial infections.[16] Prolonged length of stay can

Table 3 Outcomes of Patients with CSF Diversion Based on the Severity of Tuberculous Meningitis and the Glasgow Outcome Scale

Degree of Tuberculous Meningitis (MRC Staging)	Glasgow Outcome Scale (n=14)				
	Death	Poor Functional Outcome		Good Functional Outcome	
	GOS 1	GOS 2	GOS 3	GOS 4	GOS 5
I	0	0	0	0	0
II	3	0	1	3	5
III	2	0	0	0	0

Note: GOS= Glasgow outcome scale; Poor functional outcome was designated as a GOS 2 and 3; Good functional outcome was for scales of 4 and 5

Table 4 Outcome of Patients without CSF Diversion based on the Severity of Tuberculous Meningitis and the Glasgow Outcome Scale

Degree of Tuberculous Meningitis (MRC Staging)	Glasgow Outcome Scale (n=41)				
	Death	Poor Functional Outcome		Good Functional Outcome	
	GOS 1 n (%)	GOS 2 n (%)	GOS 3 n (%)	GOS 4 n (%)	GOS 5 n (%)
I	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
II	17 (41)	1 (2)	1 (2)	3 (7)	9 (22)
III	9 (22)	0 (0)	0 (0)	1 (2)	0 (0)

Note: GOS= Glasgow outcome scale; Poor functional outcome was designated as a GOS 2 and 3; Good functional outcome was for scales of 4 and 5

increase the risk of nosocomial infections and lead to poor outcomes.[17] However, our study found that there was no difference in the proportion regarding the incidence of nosocomial infections in patients with CSF diversion and those without. Hence, the proportion of deaths in patients without CSF diversion due to neurological reasons was higher than in those with CSF diversion. This is related to the existence of patients who refuse the CSF diversion procedure. From a total of 10 patients who refused CSF diversion, 80% died with the most common cause of death due to neurological causes.

There was a difference in outcome between patients who underwent CSF diversion and those who did not. A total of 8 of 14 patients who underwent CSF diversion had a good functional outcome. Meanwhile, only 31% of patients without CSF diversion had a good functional outcome, as opposed to the previous study conducted in Malaysia,[15] stating that patients who underwent CSF diversion procedure had a worse outcome than patients who only received drug therapy due to the delay in the patients referral to the neurosurgery department and thus the disease is at an advanced stage.[15]

In this study, the good outcome in patients undergoing CSF diversion may be related to several things. It is known that the Vellore score IV (the condition of the patient in a coma state with abnormal posture) is associated with a poor outcome.[6] In our study, no initial consciousness level of coma was found. In addition, the duration of time between the patients admitted to the hospital and the implementation of CSF diversion procedure in most patients was <1 day. In pediatric patients, suffering from tuberculous meningitis and hydrocephalus with 'early shunt' (<2 days), had a better outcome than 'late shunt' (>2 days).[18] These may be related to the high number of good functional outcome in patients undergoing CSF diversion.

The number of patients who died was 56%. This mortality proportion is similar to a previous study conducted in Northern Taiwan.[3] This study found that the mortality rate in patients who did not undergo CSF diversion was higher than in those who underwent CSF diversion. Apart from refusal of CSF diversion procedure, as previously stated, another possible cause of mortality in patients without CSF diversion is non-neurological causes such as nosocomial infection. Whereas of the total people who underwent CSF diversion, 5 of 14 patients died with a median length of stay of

12 days (IQR 9–64), and it was known that the cause of death was mostly due to non-neurological causes.

Limitation in this study is due to incomplete data since this is a retrospective study. Prospective analytical methods with more complete and accurate data at specific times might provide more insight for the treatment outcomes after a certain period of time.

This study concludes that most tuberculous meningitis patients with hydrocephalus, admitted in Dr. Hasan Sadikin General Hospital 2018, with or without the cerebrospinal fluid diversion procedure, are at an advanced stage with a high mortality rate. The proportion of good functional outcomes in patients undergoing the cerebrospinal fluid diversion is higher than patients without the cerebrospinal fluid diversion.

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