

Original Article

## Risk factors and outcomes of cerebrospinal fluid overdrainage in HIV-negative patients with cryptococcal meningitis after the ventriculoperitoneal shunting procedure

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KEYWORDS CSF overdrainage; HIV-Negative cryptococcal meningitis; Outcome; Risk factor; Ventriculoperitoneal shunt procedures	Abstract <i>Purpose:</i> Shunt procedures used to treat cryptococcal meningitis complicated with hydrocephalus and/or increased intracranial pressure (IICP) could result in cerebrospinal fluid (CSF) overdrainage, thereby presenting therapeutic challenges. <i>Methods:</i> We analyzed the clinical features and neuroimaging findings after the ventriculoper- itoneal (VP) shunt procedure in 51 HIV (Human Immunodeficiency Virus)-negative patients with cryptococcal meningitis, to assess the risk factors associated with post-shunt CSF overdrainage.
	<i>Results:</i> Symptomatic CSF overdrainage occurred in 12% (6/51) of patients with cryptococcal meningitis who underwent the shunt procedure. Rapid deterioration of neurological conditions was found in 6 patients after the shunt procedure was performed, including disturbed consciousness, quadrinaresis, and dysphasia in 5 patients and severe ataxia in 1. The mean

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duration of CSF overdrainage after the shunting procedure was 2–7 days (mean 4 days). The mean interval between meningitis onset to shunting procedure remained independently associated with CSF overdrainage, and the cut-off value for predicting CSF overdrainage in interval between meningitis onset to shunting procedure was 67.5 days.

*Conclusions:* CSF overdrainage after the VP shunt procedure is not rare, especially in patients with a high-risk of cryptococcal meningitis who also have a prolonged duration of hydrocephalus and/or IICP.

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## Introduction

Cryptococcal meningitis remains a potentially fatal central nervous system infection despite the advances in neurosurgical techniques, anti-fungal agents, and imaging technologies<sup>1-3</sup> In clinical practice, uncontrollable increased intracranial pressure (IICP) and hydrocephalus are two complications of cryptococcal meningitis. Delays in diagnosis and treatment are directly related to poor outcomes including various degrees of residual neurological sequelae.<sup>1-4</sup> Since the early 1980s, ventriculoperitoneal (VP) shunt has been used to relieve hydrocephalus or uncontrollable IICP resulting from cryptococcal meningitis.<sup>4–7</sup> However, shunt procedures do not result in good outcomes for all patients.<sup>5,6</sup> These procedures can result in shunt infection, CSF overdrainage, or shunt malfunction.<sup>1-6</sup> Furthermore, the criteria used to determine patients who require shunt procedures remains unclear.

Previous studies have focused on either children or adult patients with normal-pressure hydrocephalus.<sup>8–13</sup> To our knowledge, no study has examined the clinical features of CSF overdrainage in HIV-negative patients with cryptococcal meningitis after the ventriculoperitoneal shunting procedure. This hospital-based study may provide accurate information on the degree of hydrocephalus and IICP in patients with cryptococcal meningitis, the effects of the VP shunt procedure on neurological and functional outcomes, and post-shunt complications. Owing to the possible benefits of VP shunts in reducing functional morbidity, there is a need for better delineation of potential complications and outcomes in hospitalized patients who receive VP shunt treatment. This study presents the clinical experiences and analyzes the clinical features, neuroimaging findings, and clinical scores after the VP shunt procedure in 51 HIV-negative patients with cryptococcal meningitis who had hydrocephalus or uncontrollable IICP.

### Patients and methods

#### Study population

The medical records of HIV-negative patients with cryptococcal meningitis admitted to Kaohsiung Chang Gung Memorial Hospital were reviewed for blood cultures, microbiological records, and neuroimaging findings by using pre-existing standardized evaluation forms.

### Diagnostic criteria for cryptococcal meningitis

HIV-negative patients with cryptococcal meningitis were included if they matched any of the following criteria: (1) *Cryptococcus neoformans* detected in one or more CSF samples, (2) positive titer for CSF cryptococcal antigen, (3) clinical features of meningitis detected using CSF India ink staining, or (4) *C. neoformans* detected in blood cultures with clinical presentations of meningitis and typical CSF features.<sup>1</sup> In this study, 51 of the 180 patients who underwent the VP shunt procedure were enrolled. The hospital's Institutional Review Committee on Human Research approved the study protocol (IRB 97-0467B).

## Definitions of hydrocephalus and uncontrollable intracranial hypertension

All patients underwent brain computed tomography (CT) in the emergency room. Follow-up brain CT and/or magnetic resonance imaging (MRI) was performed post-surgery if clinical deterioration was observed, such as acute onset focal neurological deficits, seizures, status epilepticus, or progressively disturbed consciousness. Hydrocephalus was judged retrospectively on the basis of dilation of the temporal horn of the lateral ventricle and/or an Evans' index of > 0.3 as measured by an initial CT scan. Evans' index is the ratio of the ventricular width of the bilateral frontal horn to the maximum biparietal diameter. Uncontrollable IICP is defined as an extremely high opening pressure (> 350 mm  $H_2O$ ) and failure to control IICP symptoms through frequent lumbar punctures and other medical approaches such as the use of corticosteroids, mannitol, or acetazolamide.<sup>14</sup> Typically, programmable VP shunts or anti-siphon VP shunts are used to prevent CSF overdrainage, but it could cause shunt obstruction in patients with meningitis. Our standard protocol was to choose non-programmable VP shunts for patients with meningitis to decrease the possibility of obstruction after the VP shunt procedure was completed. CSF overdrainage is defined as an excessive removal of a patient's CSF using a shunt in a patient. This condition can present relatively early after shunt insertion, along with subdural effusion or hematoma.<sup>11</sup>

#### Statistical analysis

Two separate statistical analyses were performed. First, the risk factors including interval between meningitis onset

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