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# Cryptococcal Infection of the Ventriculoperitoneal Shunt in an Immunocompetent Patient

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

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**Conflict of interest:** None declared

**Patient:** Male, 52  
**Final Diagnosis:** Cryptococcal ventriculoperitoneal shunt infection  
**Symptoms:** Confusion • fever • Lethargy  
**Medication:** Amphotericin B • Flucytosine  
**Clinical Procedure:** Ventriculoperitoneal shunt removal  
**Specialty:** Infectious disease

**Objective:** Rare disease  
**Background:** Ventriculoperitoneal shunting is an effective treatment for hydrocephalus. Ventriculoperitoneal shunt (VPS) infection is a common complication. *Cryptococcus neoformans* as an implicated organism is rare. In this report, we describe a patient with cryptococcal VPS infection.

**Case Report:** A 52-year-old male with normal pressure hydrocephalus, status post implantation of VPS one year prior to the presentation; who was admitted with a fever, lethargy and confusion for three days. He was treated empirically with intravenous cefepime and vancomycin for VPS infection. The CSF analysis from both the lumbar puncture and the VPS was significant for a low white blood count, low glucose and high protein. Other work-up including India ink and cryptococcal antigen was unrevealing. He remained febrile despite antibiotic treatment for 5 days. The CSF from the shunt was sent for analysis again and it demonstrated similar results from the prior study, but the culture was now positive for *Cryptococcus neoformans*. The patient was started on oral flucytosine and intravenous liposomal amphotericin B. The VPS was removed and an externalized ventricular catheter was placed. The patient showed rapid resolution of the symptoms.

**Conclusions:** To date, there was a total of nine reported cases of cryptococcal VPS infection upon review of the literature. Our presenting case and the literature review highlight the difficulties in making an accurate diagnosis of cryptococcal shunt infection. There were case reports of false negative cryptococcal antigen tests with culture proven cryptococcal meningitis. The CSF culture from the shunt remains a mainstay for identifying cryptococcal shunt infection. Cryptococcal shunt infections are rare and early diagnosis and treatment is essential for patient management which involves shunt replacement with concomitant administration of intravenous antifungal medication. High clinical suspicion is crucial and shunt culture preferably from the valve is recommended.

**MeSH Keywords:** Central Nervous System Fungal Infections • Cryptococcus • Ventriculoperitoneal Shunt

**Full-text PDF:** <http://www.amjcaserep.com/abstract/index/idArt/896171>

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## Background

Ventriculoperitoneal shunting is a commonly used method to drain the excess cerebrospinal fluid from the cerebral ventricles into the peritoneal space in patients with hydrocephalus [1]. While VPS is effective in reducing morbidity and mortality, it also has complications. VPS infection is a common complication, with an incidence of 2% to 12% [2–4]. Bacteria such as coagulase-negative staphylococci are the most commonly implicated organism [4–7]. *Cryptococcus neoformans* as a pathogen of VPS infections is rare and the diagnosis using CSF from the shunt can be particularly difficult [8–10]. In immunocompetent patients, cryptococcal antigen tests may be negative, which makes the diagnosis more challenging [11,12]. We present the case of an immunocompetent patient who was diagnosed with culture-proven *Cryptococcus neoformans* VPS infection.

## Case Report

The patient was a 52-year-old man with a past medical history significant for normal-pressure hydrocephalus, status post-implantation of VPS 1 year prior to the presentation, who was admitted with fever, lethargy, and confusion for 3 days.

On physical examination, he was febrile, with a temperature of 101.7°F. The patient was alert and oriented to person and place only. There was no neck rigidity or focal neurological deficits, and Kernig and Brudzinski signs were negative. The physical exam was otherwise unremarkable.

A clinical diagnosis of VPS infection was made, and the patient was started empirically on intravenous cefepime 2 g every 12 h and vancomycin 15 mg/kg every 8 h. The serum white blood cell count was  $8.3 \times 10^3/\text{dL}$  and C-reactive protein was 14.4 mg/dL. A computed tomography (CT) scan of the head showed ventriculomegaly with possible shunt malfunction. CSF obtained from a lumbar puncture and the VPS were sent for culture. The CSF analysis from the shunt was significant for a low white blood cell count (WBC), low glucose, and high protein (Table 1). The opening pressure from the lumbar puncture was within normal limits. India ink microscopy was negative for capsulated organism. The cultures from both sources remained negative for 7 days. In addition, latex agglutination for cryptococcal antigen was negative.

The patient underwent a shunt revision with externalization of the peritoneal catheter on day 2. He remained febrile despite 5-day antibiotic treatment. Further investigation, including CSF acid-fast bacilli smear, Lyme DNA polymerase chain reaction, and Venereal Disease Research Laboratory (VDRL) were all negative. The CSF from the shunt was sent for analysis again and it demonstrated similar results from the prior

**Table 1.** Summary of the present case and available data on 9 cases of Cryptococcal VPS infection in the English literature.

Sex	
Male	9
Female	1
Age, mean ± age	45±14
Co-morbidities, n (%)	
Cirrhosis	1 (10)
Small cell cancer	1 (10)
Sarcoidosis	1 (10)
Duration from VPS placement to infection	
Duration from VPS placement to infection >1 year, n (%)	1 (11.1)
Duration from VPS placement to infection ≤1 year, n (%)	8 (88.9)
	1 case NR
VPS cerebrospinal fluid analysis	
WBC >10 cells/uL, n (%)	4/8 (50)
	2 cases NR
Glucose <50 mg/dl, n (%)	6/9 (66.7)
	1 case NR
Total protein >40 mg/dl, n (%)	9/9 (100)
	1 case NR
Cryptococcal antigen test positive, n (%)	4/6 (66.7)
	4 cases NR
Cryptococcal Culture, n (%)	10/10 (100)
Treatment	
Amphotericin B and flucytosine only, n (%)	9 (90)
Removal of shunt, amphotericin B and flucytosine, n (%)	8 (80)
Mortality attributed to Cryptococcal VPS infection, n (%)	4 (40)

VPS – ventriculoperitoneal shunt; WBC – white blood count; NR – not reported.

study, but the culture was now positive for *Cryptococcus neoformans*. Human immunodeficiency virus (HIV), hepatitis B, and hepatitis C screening were non-reactive. The patient denied any malignancy, organ transplantation, or long-term glucocorticoid therapy.

The patient was started on oral flucytosine 25 mg/kg every 6 h and intravenous liposomal amphotericin B 15 mg/kg daily. A repeat culture revealed persistent *Cryptococcus neoformans*. The VPS was removed and an externalized ventricular catheter

was placed. Multiple CSF cultures after shunt removal were negative. The patient continued to improve clinically and remained afebrile. He completed a 2-week induction phase with flucytosine and amphotericin B, followed by an 8-week course of per oral fluconazole 800 mg daily. A new VPS was placed 3 weeks after the original VPS was removed.

## Discussion

In this paper, we presented an immunocompetent patient with culture-proven cryptococcal VPS infection. Cryptococcal infection is a rare etiology of VPS infection. Our review of the literature showed that there have been a total of 9 reported cases [8,9].

The CSF profile of cryptococcal meningitis in HIV-negative patients has a median WBC, protein, and glucose of 73 leucocytes/mm<sup>3</sup>, 100 mg/dl, and 42 mg/dl, respectively [13]. The interpretation of CSF parameters of device-related infection is challenging and may be different from meningitis in HIV-negative patients. There is no single CSF parameter proposed to consistently predict cryptococcal VPS infection [14].

Table shows that 50% of patients had an elevated CSF WBC (>10 cells/uL), 66.7% had low CSF glucose (<50 mg/dl), and all the patients had high protein (>40 mg/dl). The CSF cryptococcal antigen tests were negative in 2 patients. Although cryptococcal antigen agglutination test of CSF samples has a sensitivity of 100% and a specificity of 95% to 100%, there were case reports of false-negative cryptococcal antigen test results with culture-proven cryptococcal meningitis [6,15,16]. It was thought that this could be a result of low cryptococcal antigen concentrations in the CSF and also is dependent on the type of test kit used [6,11,12]. Other reported causes of negative cryptococcal antigen test results include prozone phenomenon [17] and isolation of small colony variant of *Cryptococcus neoformans* [18].

Table 1 also shows that CSF cultures from the shunt were positive for *Cryptococcus neoformans* in all the patients. The presented case is unique because the CSF culture from the shunt was initially negative but a second sample grew *Cryptococcus*

*neoformans*. According to some studies, there had been reports that revealed failures to isolate causative agents in the cultures [11,19]. Nevertheless, the CSF culture from the shunt remains a mainstay for identifying cryptococcal shunt infection [7,15]. Desai et al. suggests holding the shunt culture for 10 days to allow adequate pathogen recovery time [20].

We would like to acknowledge the limitations of our case report. Our patient may have been infected during the shunt revision, which caused the repeat culture to be positive. However, the patient's clinical presentation did not improve despite broad-spectrum antibiotics and shunt revision. The repeated CSF analysis from the shunt showed a similar result after the shunt revision. Therefore, nosocomial cryptococcal infection was less consistent. The latency time from contamination to symptoms is highly variable, ranging from 30 days to more than a year [20]. Table 1 shows that 88.9% of reported cryptococcal VPS infections occurred less than a year after the VPS placement.

## Conclusions

Cryptococcal shunt infections are rare. Early diagnosis and treatment are essential for patient management, which involves shunt replacement with concomitant administration of intravenous antifungal medication. Our presented case and the literature review highlight the difficulties in making an accurate diagnosis of cryptococcal shunt infection. High clinical suspicion is crucial and shunt culture, preferably from the valve and reservoir, is recommended [21].

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## Conflict of interest

No conflict of interests exists in reporting this case for the authors.

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