

## Case Report

# Cryptococcal Meningitis Complicated by Takotsubo Cardiomyopathy: A Case Report

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## Abstract

Takotsubo Cardiomyopathy is defined as decrease in myocardial contractility in areas that do not correspond to coronary distributions. Traditionally thought of as a disease that is precipitated by acute emotional distress, it has also been observed in a variety of neurological conditions associated with increased intracranial pressure, including subarachnoid hemorrhage, stroke, and head trauma. In this report, we present the case of a 47 year old male with a history of HIV and medication noncompliance admitted to the hospital for fulminant cryptococcal meningitis. The patient's clinical course was complicated by a mid-ventricular variant of Takotsubo Cardiomyopathy seen on echocardiography. To the best of our knowledge, this is the first reported case of cryptococcal meningitis complicated by Takotsubo Cardiomyopathy.

**Keywords:** Cryptococcus meningitis, Takotsubo, Stress induced cardiomyopathy, Increased intracranial pressure

## Abbreviations

HIV: Human Immunodeficiency Virus; CSF: Cerebrospinal Fluid; CT: Computed Tomography; CC: Cubic Centimeters; EKG: Electrocardiogram; ACS: Acute Coronary Syndrome; ICP: Intracranial Pressure

## Case Presentation

A 47 year old gentleman with history HIV and noncompliance with medications presented to the emergency department after momentarily losing consciousness while driving. He also complained of a weeklong history of subjective fevers, confusion, and headache. In the emergency department, he had a witnessed complex partial seizure lasting 1 minute, with return to baseline soon after. After a computed tomography scan figure 1 showed no acute intracranial process, a lumbar puncture was performed, which revealed an elevated opening pressure of 55 cm H<sub>2</sub>O, low CSF glucose, high CSF protein, and increased nucleated cells with lymphocytic predominance (Table 1). Cryptococcal antigen test was positive.

The patient was diagnosed with cryptococcal meningitis and treated with amphotericin and flu cytosine. Leviteracetam was started for seizures. While the patient's confusion improved slightly over the next 48 hours, he spiked high fevers in the range of 38.5-39 °C. Repeat Lumbar punctures on hospital stay days 2 and 3 showed high opening pressures of 38 and 55 respectively. Due to concerns of increased intracranial pressure, the patient was transferred to the Neurological Intensive Care Unit.

Shortly after transfer, the patient developed significant tachycardia with heart rates in the range of 130-150 beats/min. EKG was done which showed sinus tachycardia with QT prolongation (interval of 553) and T wave inversions in leads me, avL, and V4-V6 without ST elevations. Troponins were significantly elevated (3.03 >2.26 >2.23 levels). Tran thoracic echocardiogram revealed global hypo kinesis with relatively conserved contractility in the apical and basilar regions.

Given the echocardiography findings, the patient was diagnosed with a mid-ventricular variant of Takotsubo Cardiomyopathy. Due to a low suspicion of acute coronary syndrome, the patient was managed conservatively and his supraventricular tachycardia was treated with metoprolol.

On day 4, the patient had an episode of acute agitation and confusion. He was given a dose of fentanyl, which improved his agitation. Later, due to the persistently high opening pressures on the previous lumbar punctures, a lumbar drain was placed and set to remove 30 cc per hour. The patient was also given a dose of Mannitol and then started on hypertonic saline with a goal sodium between 145-150 was started for cerebral edema.

Despite our interventions, the patient's mental status continued to worsen. He became disoriented to time, place, and self and was unable to follow commands. On day 5, he became suddenly unresponsive and had extensor posturing on exam. Glasgow coma scale was 4 (E1V1M2). He was emergently intubated. A stat CT showed ventriculomegaly suggestive of early communicating hydrocephalus. The patient was given another bolus of hypertonic saline to reduce cerebral edema. Due to continued escalation of nucleated count on his CSF, therapy was escalated by starting intrathecal amphotericin. Additionally, vancomycin, cefepime, and ampicillin were added according to infectious disease recommendations for possible superimposed bacterial infection based on CSF studies (Table 1).

Despite these measures, the patient's clinical condition did not improve. The patient became hypotensive, requiring use of norepinephrine. Given the patient's condition, the family decided to withdraw care and the patient expired shortly after.

## Discussion

Cryptococcal meningitis is an AIDS defining illness which typically presents as subacute meningo-encephalitis with symptoms of headache, fever, malaise, and in later stages, visual changes

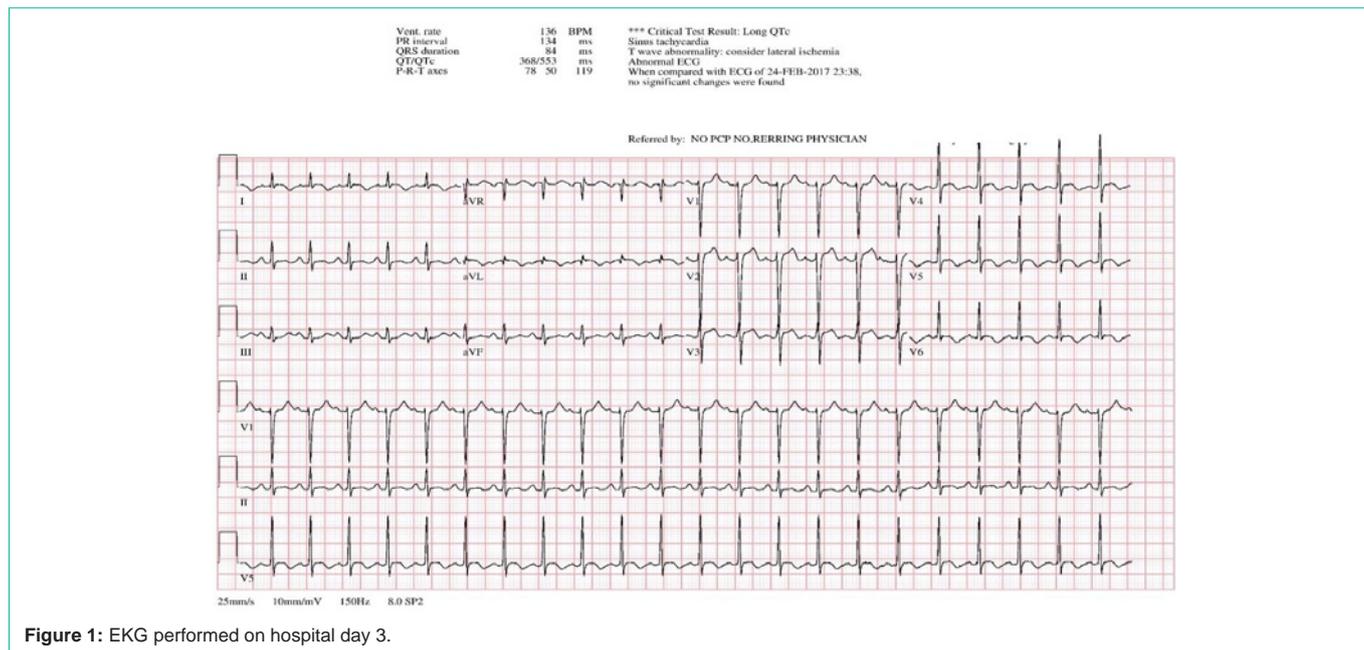


Figure 1: EKG performed on hospital day 3.



Figure 2: Transthoracic Echocardiogram.

Table 1: Lumbar puncture results.

Date	Fluid appearance	Opening Pressure	Nucleated Cells	RBC	Glucose	Protein
2/22	Hazy, colorless	55	45 (87% lymphocytes)	20	15	89
2/23	Hazy, colorless	38	5 (75% lymphocytes)	250	18	84
2/24	Clear, colorless	55	9	386	21	67
2/25	Hazy, colorless		1437 (84% neutrophils)	310	3	279
2/27	Cloudy, yellow		4256 (82% neutrophils)	230	2	602

abnormalities of T wave inversions (“cerebral T waves”) in the lateral leads as well as prolonged QT interval (Figure 2).

Although Takotsubo is typically thought of as acute cardiac dysfunction precipitated by emotional distress, there is a well-known connection between left ventricular systolic dysfunction and elevated ICP that presents very similarly [2]. Most documented cases involve elevated ICP in the setting of subarachnoid hemorrhage [4], but there are also reports related to ischemic stroke and head trauma [5,6]. The proposed pathophysiological mechanism involves increased ICP and neurological stress activating the sympathetic nervous system and causing excess amounts of catecholamines to be released. The apical surface (or in other variants, mid-ventricular or basal regions) of the heart has a higher concentration of adrenergic receptors, which becomes transiently stunned with the surge of catecholamines, leading to the regional wall abnormalities seen on imaging [7].

No standardized treatment approach to stress-induced cardiomyopathy exists. Cardiac dysfunction is typically temporary [8] and will normalize with resolution of the underlying cause. As most cases present similar to acute MI, ACS protocol is often initiated and most patients receive standard acute coronary syndrome therapy [9]. Since pathophysiology involves a surge of catecholamines, there is a theoretical argument for the use of beta blockers, but while they have been shown to benefit in cases of mid-ventricular obstruction

and altered mental status [1]. Severe cases may result in elevated intracranial pressure (ICP) [1]. Rarely, cryptococcal meningitis may follow a fulminant course. Although cardiac abnormalities have not been associated with cryptococcus meningitis particularly, there are many reported cases that document a connection between elevated ICP and cardiac dysfunction [2]. Here, we report what to our knowledge is the first case of fulminant cryptococcal meningitis complicated by Takotsubo Cardiomyopathy in a 47 year old male with AIDS.

The diagnosis of Takotsubo Cardiomyopathy was made in accordance with Mayo Clinic’s diagnostic criteria [3], which requires decreased contractility and regional wall abnormalities extending beyond a single vascular distribution in the absence of coronary artery disease, pheochromocytoma, or myocarditis, alongside new ST-segment elevation and/or T-wave inversion or modest elevation cardiac troponins. In this case, echocardiographic findings revealed hypo contractile pattern predominant in the mid-ventricular region. In addition, our patient had elevated troponins and EKG

and hypotension [10], there is no evidence they reduce either primary incidence or recurrence of Takotsubo [11]. If cardiogenic shock develops, catecholamines like dobutamine are generally avoided for reasons related to the pathophysiologic mechanism.

In summary, this case highlights the fulminant nature of cryptococcal meningitis which can be associated with Takotsubo cardiomyopathy and the challenges in its treatment. To our knowledge, this is the first case to report the association between Cryptococcal meningitis and Takotsubo Cardiomyopathy. Treatment must be individualized to each patient and involves heart failure & hemodynamic management, alongside attempts to reduce ICP.

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