



Fungal Meningitis in an Allegedly Immunocompetent Patient in Sri Lanka: A Case Report

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ABSTRACT

Fungi are a significant source of microorganisms, which cause disability and death. They act as opportunistic pathogens in the immunocompromised host. Though it is rare among immunocompetent patients, a 44-year-old allegedly immunocompetent woman developed a sudden onset of headache which was holocranial but radiated to the occipital and neck region gradually and ended up with altered agitated behavior and presented to the Emergency Treatment Unit of National Hospital of Sri Lanka. Cerebrospinal fluid analysis revealed the diagnosis of probable Cryptococcal meningitis. Despite free health care system for every citizen of the country with the current economic burden, the management of prevailing treatment became complicated. Administering IV Conventional amphotericin B instead of the ideal treatment of IV Lymphosomal Amphotericin B showed numerous side effects and toxicity systemically in general and specifically on the genitourinary tract of the patient. At the same time, it opened access to a debatable question on assessing the value of disease-centered care and holistic approaching methods especially for the health care professionals. Meanwhile, this study discusses the assessment and implementation of nursing care

considering the complications of drug toxicity and adverse effects combined with psychologically negative behavior due to prolonged hospitalization for more than 35 days. This case study reveals the impact of nurses' knowledge and understanding in providing care for the management of rare diseases like fungal meningitis. To provide comprehensive care nurses and the health care team must work together with updated knowledge and hands-on skills for a better patient outcome.

1. INTRODUCTION

Fungal infections in the Central Nervous System (CNS) though rare become significantly increasing in statistics all over the world due to immunosuppressive diseases like Human Immunodeficiency Virus (HIV), Tuberculosis and the advancement of therapies for organ transplants and defeating carcinoma (Kumar & Priyanka, 2018). *Cryptococcus* is an encapsulated yeast, an opportunistic fungal pathogen that may lead to life-threatening infections such as meningoencephalitis and disseminated cryptococcosis, usually in immunocompromised hosts (Jha et al., 2019). However, it is rarely considered when dealing with patients who are immunocompetent (Nathan et al., 2021) as someone with a healthy immune system very rarely develops cryptococcal meningitis (Centers for Disease Control and Prevention, 2019). The infectious agent is commonly found in soil contaminated by pigeon droppings. Infection by this organism is typically isolated from the lungs or lymph nodes but hematogenous spread can result in infection of other organ systems such as the nervous system (Nathan et al., 2021). *Cryptococcus* is the most common cause of fungal meningitis in both the immunocompromised and immunocompetent hosts (Nathan et al., 2021). The preferred Antifungal therapy for cryptococcal meningitis consists of intravenous amphotericin B plus flucytosine. Immunocompetent patients who present with mild-to-moderate symptoms should

be treated with fluconazole, 200–400 mg/d for 6–12 months (Dismukes et al., 1987). When fluconazole is not an option, itraconazole (200–400 mg/day) is the acceptable alternative regimen (Denning et al., 1989). When flucytosine was added to amphotericin B as a combination therapy, the overall outcome was improved and the duration of treatment could be reduced from 10 weeks to 4–6 weeks (Dismukes et al., 1987). It consists of induction, consolidation, and maintenance phases of therapy (Hesarur et al., 2021).

This case presents a patient who was allegedly immunocompetent, though diagnosed with cryptococcal meningitis. The initial Cerebral-Spinal Fluid (CSF) test showed positive for organisms with elevated protein and decreased glucose levels. The management became complicated when the existing economic crisis came into account despite free healthcare accessible system in Sri Lanka. The unavailability of ideal treatment and use of conventional amphotericin B and the series of side effects show how it is influencing the economic burden on the health care system in a country.

Nurses who cater to the needs of this type of patients with rare conditions should be more knowledgeable and experienced in caring for and managing these conditions making positive end results. They must be able to identify the uniqueness of this fungal meningitis compared to the other types of meningitis as well as in-depth knowledge of standard treatment regimens and nursing care with special attention to the psychological needs of clients when they demonstrate anxious behaviors. The nurse is obliged to preserve the rights of the patient to refuse the treatment with the disagreement of continuation of IV amphotericin B due to a series of side effects and the same time make aware of the importance of continuation of the treatment as well.

2. CASE PRESENTATION

A 44-year-old woman who is a mother of two children, an IT officer by occupation in a government university from a suburban area of Sri Lanka, developed a sudden onset of headache during her working hours. That was holocranial but radiated to the occipital and neck region gradually and ended up with altered behavior within a short period of time and then presented to the Emergency Treatment Unit, National Hospital of Sri Lanka, in June 2022. This was associated with talking incomprehensibly, disoriented, and progressively agitated behavior. About one week back she encountered the same episode and was admitted to a local nongovernmental hospital where she is treated for migraine. She recovered spontaneously within the hospital and worked up for routine investigations. Her reports were found to be normal except for one blood report (ESR – 115mm) and suggested undertaking an MRI brain which revealed multiple sub-cortical hyperintensities from chronic ischemic changes (correlate with early small vessel disease or could be due to migraine). She was informed to be admitted to a hospital to follow further investigations and suggested following a series of treatments. She did not follow the instructions at that time, remained at home and suddenly developed the above symptoms. In terms of her health history, she suffered from recurrent headaches for 3 months following being infected with COVID-19 in March 2022. She has only taken her two doses of COVID-19 vaccination. Further, she was diagnosed with migraine and there were no significant health issues other than that. There was also no history of tuberculosis. She was with an Intra Uterine Copper Device (IUCD) and never used oral contraceptives. As per the client's statement, she was not from an environment surrounded by pigeons; only raised a dog as a pet in her home but kept it away from indoor premises.

On her clinical assessment, her Blood Pressure

(BP) was 126/73mmHg, body temperature was 98.4°F, afebrile, Pulse Rate (PR) = 91 min⁻¹, Oxygen Saturation = 99%, lungs clear, abdomen soft, her Glasgow Coma Scale was 12/15, Pupils Equal and Reactive to Light (PERL) and her other neurological assessments were normal. Started management as differential diagnosis as viral or autoimmune encephalitis and administered antiviral drugs (IV acyclovir 500mg 8H, IV Cefotaxime 2g 8H) due to high value of creatine phosphokinase (CPK=1293). All of these laboratory parameters are shown in Table 1.

Table1: Laboratory parameters

Parameter	Value	Normal ranges
Complete Blood Count		
- White blood cell	11.64 X10⁹/L	4-10 X10 ⁹ /L
- Neutrophils	76 %	55-70%
- Lymphocytes	37 %	20%-40%
- Monocyte	1 %	2%-8%
- Eosinophil	2%	0-6%
- Red blood cells	4.8× 10 ¹² /L;	(4.2–5.4)L
- Hemoglobin	9.4 g/dL	(12-15) g/dL
- Platelets	292 X 10 ⁹ /L	(150-400) X 10 ⁹ /L
Biochemistry		
Random blood sugar	125 mg/dL	(79-160) mg/dL
Urea	28 mg/dL	(17-45) mg/dL
Creatinine	0.81 mg/dL	(0.8-1.3) mg/dL
Sodium	135 mmol/L	(135-145) mmol/L;
Potassium	3.8 mmol/L	(3.5 – 5) mmol/L
Calcium	8.5 mg/dL	(8.4-10.2) mg/dL
Albumin	3.4 gm/dL	(3.5-4) gm/dL
Magnesium	1.4 mg/dL	(1.6-2.3 mg/dL)
Amylase	44 U/L	(30-125) U/L
ESR	115 mm/hr	<15mm/hr
CRP	29.3 mg/dL	<0.3mg/dL
CK	1293 U/L	Female 30-145U/L Male 55- 170U/L
TSH	1.386 mIU/L	0.4- 4.0mIU/L
T ₄	1.113 µg/dL	5- 12µg/dL

Hepatic panel		
Bilirubin total	0.8mg/dL	0.1-1.2 dL
direct	0.5 mg/dL	0-0.4 mg/dL
ALT	24 units/L	5-30 units/L
AST	40 units/L	5-30 units/L
Alkaline Phosphatase	76 IU/L	50-100 IU/L
Cerebrospinal fluid (CSF) analysis		
Red Blood Cells	4mm ³	0-10/mm ³
White Blood Cells	Absent	0-5/mm ³
Protein	390 mg/dL	20-45 mg/dL
Sugar	19 mg/dL	45-80 mg/dL
Lactate	2 mmol/L;	1.1-2.8 mmol/L;
Lymphocytes	26 H.P.F	1-5 /H.P.F
GeneXpert	was negative for Mycobacterium Tuberculosis	
CSF India ink staining	Capsulated yeast	
Bacterial culture	Positive over 48 hrs; Cryptococcus spp. present	

Plain Computed Tomography (CT) of the head was normal (figure 1). Serological test for HIV 1 and HIV2 Ab +Ag were negative. HSV PCR type 1& 2 not detected. The Mantoux test was negative.

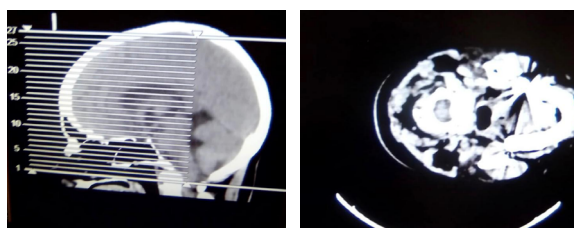


Figure 1: NCCT BRAIN

With the diagnosis of cryptococcal meningitis, microbiologists' opinion was to administer Intravenous liposomal amphotericin B (3 mg/kg /day) along with IV fluconazole (1200mg daily) and IV ceftriaxone (2g/8H). Unfortunately, the liposomal amphotericin B was not available in the stocks. Even though Sri Lanka has a state-funded healthcare system, free of charge to each citizen,

the government was unable to afford liposomal amphotericin B due to the high expense of this drug instead of conventional amphotericin B (14 days drug administration regime). With the review of microbiology experts, it was started to administer conventional amphotericin B following the negative results of the sensitivity test (IV conventional amphotericin B 1mg/kg in 500ml of 5% dextrose/4H-6H). Further, it is instructed to hydrate the patient with 500ml of IV normal saline before and after the procedure. On the same day evening, her hypersensitivity reactions were evident with chills and rigors, BP=160/90mmHg, SPO2=98% on RA, PR=118, and temperature=98.6°. The infusion is stopped and managed the reactions immediately with IV Hydrocortisone 200mg (stat) and IV chloramphenicol 10mg (stat). Oxygen (4L/min) via face mask was administered while monitoring urine output and BP. She seems to not know about the importance of this drug and its side effects. The nursing officer identified her knowledge was very poor as she only knew that "the drug is more powerful". The review of the microbiology team and medical management continued with the same drug (3mg/kg/day) on day two as well. Prior to administration she was hydrated well with normal saline as per the instructions and administered IV Hydrocortisone 200mg (stat) and IV Chloramphenicol 10 mg (stat). On the third day of administration, a Central Venous Pressure (CVP) line was inserted under aseptic techniques and planned to assess K⁺, Ca²⁺, and Mg²⁺ levels daily. After the 4th day of administration, she complained about left-sided tightening-type chest pain. Then the heart function is evaluated with 2D Echo (Ejection Factor=56%, global hypokinesia), cardiac rhythm as well as cardiac enzymes (Troponin I negative), and Lipid profile test results were all normal. Administering antacids (IV pantoprazole 40mg bd) is also done. Daily renal function level reveals increases of Serum Creatinine, hypokalemia, hypomagnesemia and hypocalcemia situation (S.Cr.=2.25, K⁺=2.8, S. Ca=7.80, S=1.55 mg) on

Day 8. The Ultrasound Scan of the abdomen reveals Acute Kidney Injury (AKI) (Ultrasound Scan of Kidney Ureter Bladder- found multiple gall bladder calculi, Bi lateral Renal parenchymal changes favour AKI) therefore the IV amphotericin B administration is withheld. Restarted the drug with the review of the opinion on immunology and microbiology. Again, she developed per vaginal bleeding and was Antinuclear Antibodies (ANA) positive (1: 1286), and one pint of red cell blood pack is administered. Further, she was sent for flow cytometry. After the 12th day of drug administration, she complained about chills and rigor, fever, and settled with antipyretic drugs. Again, on day 13, she increased the symptoms: fever with dyspeptic symptoms, bilateral hand numbness, BP=120/80mmHg, PO₄=3.48. Further, it is planned to repeat lumbar puncture. On day 14 onset of fever spiked at 100.8^oF, hypokalemia, hypocalcemia, and hypomagnesemia, a sign of AKI (S.Cr. 1.60-1.51-1.82), immunocompromised with lymphopenia and anemia, ANA was also positive.

However, after completion of the induction phase, her consolidation phase (with O. fluconazole 800mg /daily, IV Piperacillin 4g/8H) started. She was complaining of nausea and loss of appetite throughout the process with severe abdominal pain. She looks anxious and the most confusing request she made throughout the process is discontinuing IV amphotericin B. Moreover, she made complaints about her left painless red eye. The ophthalmologist's opinion revealed a left subconjunctival haemorrhage in the left eye and bilateral disc edema. Eye suspension is also applied daily.

When her CSF assessment and all the other parameters were getting normal an MRI was done (figure 2) before she was discharged after staying almost more than a month; 35 days in the hospital.



Figure 2. (Impression: Prominent perivascular spaces in bilateral basal ganglia, cerebral white matter and right midbrain region, could be representing a feature of Cryptococcal meningitis. However, since these imaging findings are non-specific, clinical correlation is necessary).

On the first follow-up week following discharge, she was doing well. She was last seen in August 2022 after completing 2 weeks of oral fluconazole 800 mg daily. She was asymptomatic and clinically improving. But still complaining about pain in lower limbs and back pain as well as poor appetite. She was prescribed a daily tablet of fluconazole 800 mg for 8 weeks and the follow-up management will be altered during later visits.

3. DISCUSSION

This is the case presentation with a symptomatic allegedly immune competent probable Cryptococcal Meningitis patient who was diagnosed based on the finding of Cryptococcal antigen in her CSF. With the differential diagnosis of viral, autoimmune, and bacterial, the medical management is able to find the diagnosis within two days of admission. She seems to have no relationship with environmental contamination with the feces of pigeons, the fact she tested positive for COVID-19 may be a possible cause of transmission of the disease.

Lymphosomal amphotericin B and Flucytosine combination treatment is the standard treatment

for treating this condition (Nathan et al., 2021). However, highly expensive medicines are affordable to all citizens in the national healthcare system in Sri Lanka (Ministry of Health Sri Lanka, 2015). As recommended by Henao-Martínez et al. (2021) conventional amphotericin B has to be administered instead of Lymphosomal amphotericin B, due to the effect of the current economic crisis.

Due to lack of resources or the ideal treatment, patients lead to unbearable side effects and exposure to toxicity. The patient in this case reported encountering AKI, PV bleeding, anemia, lymphocytopenia, severe gastric enteritis, subconjunctival hemorrhage, and psychological instability with the treatment as well as the disease.

As nurses who cater to the needs of this type of rare cases, up-to-date knowledge and a handful of experience in caring and managing such conditions to make positive end results are necessary. As a team healthcare professionals must be clever enough to identify the uniqueness of this fungal meningitis compared to the other types of meningitis as well as gain in-depth knowledge on standard treatment regimens instead of only maintaining all the charts required for further surveillance as routine procedures. It is more important when it comes to a patient who continues treatment with a drug which is having a lot of side effects, especially as it is the only option for rescuing the life of the patient. The nurse should consider the psychological aspect of the client and the needs during the critical stages. The nurse is obliged to preserve the rights of the patient to refuse the treatment (Olejarczyk & Young, 2022) with the disagreement of continuation of IV amphotericin due to a series of side effects and at the same time, nurse should make the patient aware of the importance of the continuation of the treatment as well. On such occasions when hypersensitivity reactions are taking place, the nurse must make a

quick decision to withhold the drug administration and make surveillance to observe the patient while reassuring the client.

4. CONCLUSION

Cryptococcal meningitis is a challenging disease that can be associated with high mortality rates. Cryptococcal meningitis should be a considerable diagnosis for immunocompetent patients as well. In Sri Lanka, the government treatment with free health facilities for each and every person seems curtailed when treating CM patients at present. The ideal treatment for allegedly immunocompetent patients is IV Lymphosomal Amphotericin B instead of Conventional amphotericin B which showed numerous side effects for the patients in the study. With the present crisis and inflation situation, the free health care system failed to supply ideal treatment. Nurses as health care professionals who involve direct care with this type of rare cases should be more knowledgeable to give comprehensive care. In that manner, more experience and exposure in medical care settings also play a significant influence. Nurses' psychological comprehensiveness towards the patients seems greatly anticipated. Hence, it can be suggested to the management to assign more knowledgeable, well-experienced nursing professionals to provide care for these types of rare cases.

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