

# Cryptococcal Meningitis in An Immunocompetent Patient

Syed Hassan Tanvir Ramzi, Shoaib Saleem, Ubaidullah Ansari, FNU Namal, and Yasra Kiran

## ABSTRACT

A fungal illness called cryptococcal meningitis is most often thought of as an opportunistic infection that affects immunocompromised people, typically those who have HIV infection. Numerous problems are linked to it, including widespread illness and neurologic ones such as intracranial hypertension, cerebral infarcts, vision loss, and other abnormalities. Here is a case 18-year-old male patient, who presented with persistent headache and fever. A lumbar puncture revealed a cryptococcal infection in him. His workup indicated no known underlying illness that may have compromised his immune system. CSF was then tested for cryptococcal species using an Indian ink preparation, and the results were positive. He was admitted to the hospital for initiation of antifungal therapy with amphotericin B along with serial serum creatinine and electrolytes levels and after the 5<sup>th</sup> day of getting amphotericin B, he had shown remarkable improvement in total symptomatology.

**Keywords:** AIDS, CSF, cryptococcal meningitis, HIV, immunocompetent.

**Published Online:** June 30, 2023

**ISSN:** 2736-5476

**DOI:** 10.24018/ejclinimed.YEAR.Vol.Issue.ID

**S. H. T. Ramzi \***

Bakhtawar Amin Medical and Dental College, Multan, Pakistan.

(e-mail: hassantanvir58@yahoo.com)

**S. Saleem**

Ibne Sina Hospital and Research Institute, Multan, Pakistan.

(e-mail: shoaibsaleem@gmail.com)

**U. Ansari**

Ibne Sina Hospital and Research Institute, Multan, Pakistan.

(e-mail: ubaidullah0264@gmail.com)

**F. Namal**

Social Security Hospital, Faisalabad, Pakistan.

(e-mail: dr.namalilyas@gmail.com)

**Y. Kiran**

Ibne Sina Hospital and Research Institute, Multan, Pakistan.

(e-mail: yasra8@gmail.com)

*\*Corresponding Author*

## I. INTRODUCTION

An invasive fungus called *Cryptococcus* is the source of cryptococcosis, an uncommon illness that is often seen in immunosuppressed people. *Cryptococcus neoformans* and *Cryptococcus gatti* are the two species of *Cryptococcus* most often linked to infections in people. The organism is quite common in several parts of the planet. The most prevalent causes of exposure, however, are old exposure to soil and bird droppings [1].

Clinical disease in the CNS and lungs is far more likely to be brought on by *C. neoformans* and *C. gattii*. Skin, the prostate, the eyes, and the joints, are less often infected bodily parts. The ability of this yeast to spread widely and infect the majority of organs in patients with severe immunosuppression should be emphasized [2].

Cryptococcal infection in humans typically results from *Cryptococcus neoformans*, which causes mild infections ranging from airway colonization to severe diseases like meningitis or disseminated disease. The most frequent type of adult meningitis in areas with high rates of human immunodeficiency virus (HIV) infection is cryptococcal meningitis (CM). It is subacute meningitis, which mostly affects people with HIV and other immunodeficient diseases,

most notably cellular immunity that isn't working properly. According to estimates, 181 000 people per year die from cryptococcal meningitis, with sub-Saharan Africa accounting for 75% of these deaths. Furthermore, 15% of all AIDS-related fatalities worldwide are attributable to the disease. Approximately 3400 cases and up to 700 fatalities are thought to occur annually in the United States [3].

Subacute meningoencephalitis is how cryptococcal meningitis often manifests. Lethargy, fever, stiff neck, nausea, and vomiting are other signs and symptoms that the patient often exhibits, along with neurological symptoms such as headaches and altered mental state (all of which are linked to an active inflammatory response). At their first visit, some HIV-positive individuals may have few or vague symptoms. In cases of HIV, the interval between the onset of symptoms and their presentation is usually between one and two weeks, but in cases of non-HIV, it is between six and twelve weeks. Diplopia and photophobia are two early signs of the illness, while subsequent signs include reduced visual acuity (induced by high cerebrospinal fluid (CSF) pressure or compression of the optic nerve and tracts). Ataxia, aphasia, seizures, chorea, and hearing issues are further outcomes [4].

Initial assessment procedures should be based on the results of CSF lab testing. It is important to culture blood and

CSF for fungus and check for cryptococcal antigens. Even when a condition is prevalent, routine lab tests may still be normal [5]. The opening pressure at the initial spinal tap must be monitored; a pressure of more than 25 cm of water indicates a dismal prognosis. The glucose and protein levels in CSF are typically low. Lymphocytes might predominate in a white cell count that is normal or more than 20 microliters. However, India ink stain and antigen testing findings for CSF might be normal and positive [6].

Induction, consolidation, and maintenance are the three stages of treatment for cryptococcal meningitis. To improve results, more people must have access to effective treatment. Strong fungicidal medications are required for induction therapy to be effective. Antiretroviral therapy must be started at the appropriate time for patients with asymptomatic cryptococcal antigenemia who have a human immunodeficiency virus infection [6].

## II. CASE REPORT

An 18-year-old male presented to Ibne Sina Hospital and Research Institute, Multan, Pakistan in November 2022, with complaints of fever and headache for the last two months. He had developed a fever 2 months back which was low-grade, intermittent, and associated with a headache that was generalized, continuous, and severe in intensity. The headache was associated with photophobia and phonophobia only and there was no association with any fits, vomiting, nausea, diplopia, or any history of head trauma or sinusitis. Now for the last three days, he had been having worsening attacks and he had presented to us confused and drowsy. His past medical, surgical, social, and family history is nonsignificant. His General Physical exam was unremarkable and on Neurological examination, only his higher mental functions were impaired.

We planned a baseline workup and lumbar puncture after acquiring a CT scan. The CT scan was unremarkable. Lumbar reports indicated clear watery color, normal opening pressure; LDH 10.85 u/l (0-40 U/L); Glucose 72.50 mg/dl (40-74 mg/dl); proteins 26 mg/dl (20-45 mg/dl); RBC and WBC were 1/mm; total lymphocytes were 100%. CSF cytology revealed no atypical or malignant cells and gram staining also showed no organism growth. Keeping his lumbar puncture picture in mind which indicated the likelihood of fungal meningitis hence his CSF was then tested for cryptococcal species by Indian ink preparation which was positive. We had ruled out any immunodeficiency i.e. his cell lines were normal [CBC shows Hb 13.5 g/dl (13.5-18 g/dl); RBC count  $4.6 \times 10^{12}/L$  ( $4.5-6.5 \times 10^{12}/L$ ); TLC 9900/cm ( $4000-11000/cm$ ); Platelets 281,000/mm ( $150,000-400,000/cm$  and he was also negative for HIV. We started treatment with amphotericin B along with serial serum creatinine and electrolytes levels and after the 5<sup>th</sup> day of getting amphotericin B, he had shown remarkable improvement in total symptomatology. After the therapy, a repeat lumbar puncture was done, and CSF was then tested for cryptococcal species which was negative.

## III. DISCUSSION

Often, immunocompromised hosts are the ones that get a cryptococcal infection in humans, which is typically brought on by *Cryptococcus neoformans*. Over 600 000 individuals worldwide die away from the illness each year, with the yearly incidence of cryptococcal disease estimated to be 1 000 000 new cases. Although widespread infections may happen, meningitis is the most serious symptom of cryptococcal illness. According to estimates, 181 000 people each year die from cryptococcal meningitis, with sub-Saharan Africa accounting for 75% of these fatalities. Additionally, the illness is responsible for 15% of all AIDS-related fatalities globally. Approximately 3400 cases and up to 700 fatalities are thought to occur annually in the United States [7].

According to studies, *C. Neoformans* after being inhaled from the environment, avoid host macrophages by using its multiple virulence factors and phenotypic plasticity, which enables it to cross the blood-brain barrier and grow in a nutrient-poor environment. Infection with cryptococcal meningitis is primarily caused by two factors. The first is exposure to an organism at a high level, for example as bird feces where *C. Neoformans* have been found. The second is immunosuppression caused by conditions including HIV, alcoholism, diabetes mellitus, or autoimmune disease [8]. Cryptococcal meningitis is a frequent opportunistic infection in individuals with an underlying immunosuppressive state, particularly AIDS patients. However, it may occur, usually in tropical regions, in immunocompetent people. The underlying patient's condition is influenced by geographical and climatic conditions in several ways. Only one patient with cryptococcal meningitis among 94 non-HIV-infected participants in the research had no underlying illness. From Singapore, Spain, Australia, and other tropical and subtropical countries, case reports of cryptococcal meningitis in immunocompetent individuals have been documented.

In the current instance, the patient was in good health and didn't have any immunosuppressive conditions. When determining the cause of a patient's symptoms, it is important to carefully explore the wide range of possible diagnoses for headaches and altered mental states. The example described here demonstrates how a generally healthy, immunocompetent person may exhibit apparently unimportant symptoms of cryptococcal meningitis, such as headaches, before more significant signs and symptoms, like altered mental state, emerge.

The parameters currently utilized to assess a patient's likelihood of contracting cryptococcal meningitis are inadequate. Since fewer than 20% of patients with cryptococcal meningitis have the constellation of symptoms known as meningismus, a typical finding in meningitis, it might be difficult to make an appropriate diagnosis in the emergency department [9]. The majority of individuals with cryptococcal meningitis have at least one of the following symptoms: fever, nuchal stiffness, altered mental state, headache, or both. The doctor could wrongly believe that the patient has a chronic illness rather than an acute pathology when individuals who don't have the clear risk factors for cryptococcal meningitis arrive with hazy symptoms or repeatedly with the same symptoms, including headache. Thus, in otherwise healthy, immunocompetent individuals, anchoring bias presents a significant challenge to the rapid

and accurate detection of cryptococcal meningitis [10].

Following diagnosis, intravenous amphotericin B and flucytosine antifungal medicine is often used together with induction therapy to quickly sterilize the CSF. Only an infectious disease specialist should be consulted while making this decision, however. Another essential component of treating cryptococcal meningitis is lowering elevated intracranial pressure by lumbar puncture (or VP shunt) until pressure returns to normal because of the significant inflammatory burden.

A second lumbar puncture is often performed after two weeks of antifungal induction treatment to check that the CSF has been sterilized. If the CSF has been sterilized, the dose of the medication may be decreased to a consolidation dosage range, even in patients who have recovered clinically (400 mg fluconazole daily) [11]. For a year or more, fluconazole consolidation and maintenance treatment may be given. Remember that particular advice varies for different groups of people, including those with HIV, those who have had organ transplants, kids, and women who are pregnant.

Patients with cryptococcal meningitis who don't exhibit the typical meningitis symptoms and who don't have the major risk factor (immunosuppression) often have poor outcomes because diagnosis and treatment are put off. The kind of immunosuppression at play under the surface and the coexisting disease processes are the most crucial prognostic variables. Further indicators of poor prognosis include the presence of India ink in the CSF, a CSF white blood cell count < 20 L, an initial cryptococcal antigen titer of more than 1:32 in the CSF or serum, and a high opening pressure upon lumbar puncture [12].

#### IV. CONCLUSION

Although a Despite being an uncommon cause of meningitis in immunocompetent people, C neoformans meningitis should nonetheless be taken into account in patients who have headaches and mental changes because of its sneaky onset and high death rate. Every time a patient is seen, a thorough and thorough history should be taken in order to assess risk factors for severe illnesses and reduce the range of possible diagnoses.

#### ACKNOWLEDGMENT

The authors declare that they do not have any further acknowledgments.

#### CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

#### REFERENCES

- [1] Levitz SM. The ecology of Cryptococcus neoformans and the epidemiology of cryptococcosis. *Rev Infect Dis*. 1991; 13(6): 1163-9.
- [2] Kwon-Chung KJ, Fraser JA, Doering TL, Wang Z, Janbon G, Idnurm A, et al. Cryptococcus neoformans and Cryptococcus gattii, the etiologic agents of cryptococcosis. *Cold Spring Harb Perspect Med*. 2014; 4(7): a019760.

- [3] Pescador Ruschel MA, Thapa B. Cryptococcal Meningitis. *StatPearls Publishing*; 2023.
- [4] Chau TT, Mai NH, Phu NH, Nghia HD, Chuong LV, Sinh DX, et al. A prospective descriptive study of cryptococcal meningitis in HIV uninfected patients in Vietnam-high prevalence of Cryptococcus neoformans var grubii in the absence of underlying disease. *BMC Infect Dis*. 2010; 10(1): 199.
- [5] Rajasingham R, Wake RM, Beyene T, Katende A, Letang E, Boulware DR. Cryptococcal meningitis diagnostics and screening in the era of point-of-care laboratory testing. *J Clin Microbiol*. 2019; 57(1).
- [6] Iyer KR, Revie NM, Fu C, Robbins N, Cowen LE. Treatment strategies for cryptococcal infection: challenges, advances and future outlook. *Nat Rev Microbiol*. 2021; 19(7): 454-66.
- [7] Pukkila-Worley R, Mylonakis E. Epidemiology and management of cryptococcal meningitis: developments and challenges. *Expert Opin Pharmacother*. 2008; 9(4): 551-60.
- [8] Su X-H, Li W-P, Lin Q, Zheng X-J, Fang T, Jiang Y, et al. Case report: a special case of cryptococcal infection-related inflammatory syndrome in a non-HIV infected and non-transplant patient. *BMC Neurol*. 2022; 22(1): 247.
- [9] Acharya S, Yadav SK, Singh PB, Bhandari S, Gautam J, Pathak S, et al. Cryptococcal meningitis in an immunocompetent individual: A case report. *Clin Case Rep*. 2021; 9(10): e04894.
- [10] Ghasemian R, Najafi N, Shokohi T. Cryptococcal meningitis relapse in a immunocompetent patient. *Arch Clin Infect Dis [Internet]*. 2011; 6(1): 51-5.
- [11] Vu K, Garcia JA, Gelli A. Cryptococcal meningitis and anti-virulence therapeutic strategies. *Front Microbiol*. 2019; 10: 353.
- [12] Poley M, Koubek R, Walsh L, McGillen B. Cryptococcal meningitis in an apparent immunocompetent patient. *J Investig Med High Impact Case Rep*. 2019; 7: 2324709619834578.

**Dr. Syed Hassan Tanvir Ramzi**, Born in Multan, Pakistan in 1997 completed his matriculations from the beacon house school system, Multan in 2013 and his undergraduate medical degree (MBBS) from the University of Health Science, Lahore, Pakistan in 2021.

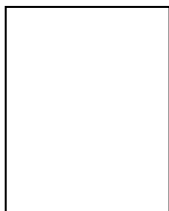
He worked in neurology during his internship years of 2022 at ibne seina hospital and research institute, Multan, along with having further experience as a medical officer in a neurological outpatient setup under the supervision of diplomates specialized in Neuromuscular Medicine. Currently, he is working in a teaching post at Bakhtawar Amin Medical and Dental College, Multan, Pakistan

He has published many works some of which are under publications including meta-analyses and case reports. Dr. Ramzi was listed in the top roll of honors during his undergraduate years in academics and has conducted public awareness drives as well.

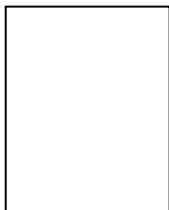
**Dr. Shoaib Saleem** was born in Multan, Pakistan in 1996, and completed his matriculation in nishat high school Multan in 2011, he completed his undergraduate medical degree from the University of Lahore, Pakistan in 2020 and completed an internship at Nishtar hospital Multan in 2020-2021. He is currently working as a medical officer at ibne seina hospital from the 16-January to date.

**Dr. Ubaidullah Ansari** was born in Multan, Pakistan on 1989 and completed his undergraduate medical studies form Punjab medical college in 2012, he completed his postgraduate training in the field of Neurology form mayo hospital Lahore, Pakistan in 2016, and joined as an associate professor in neurology in ibne seina hospital on 2018 till date.

Dr. Ansari is an active member of the Pakistan Society of Neurology.



**Dr. FNU Namal** was born in Born in Faisalabad 1996 and completed high school at DPS, an undergrad from the University of health sciences with state honors currently working in a Social Security hospital in the Department of Medicine and High dependency unit since November till date.



**Dr. Yasra Kiran** was born in Multan, Pakistan in 1996 and completed his matriculation at nishat high school Multan in 2011, she completed her undergraduate medical degree from Lahore, Pakistan in 2020 and completed an internship from Nishtar Hospital Mulan in 2020-2021. She is currently working as a Postgraduate resident trainee in internal medicine at ibne seina hospital.