Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 May 05; 10(T7):138-141.
https://doi.org/10.3889/oamjms.2022.9238
eISSN: 1857-9655
Category: *T7 - "Neuroscience, Neurology, Psychiatry and Other Health Sciences - 2022"*
Section: *Neurology*

Case Report: Cryptococcal Meningitis

Popy Paramitha, Kiking Ritarwan*

Department of Neurology, Universitas Sumatera Utara, H. Adam Malik General Hospital Medan, Medan, Indonesia

Edited by: Branislav Filipović
Citation: Paramitha P, Ritarwan K. Case Report: Cryptococcal Meningitis. Open Access Maced J Med Sci. 2022 May 05; 10(T7):138-141. https://doi.org/10.3889/oamjms.2022.9238
Keywords: Cryptococcal meningitis; AIDS; Immunocompromised
***Correspondence:** Kiking Ritarwan, Department of Neurology, Universitas Sumatera Utara, H. Adam Malik General Hospital Medan, Medan, Indonesia. E-mail: kiking@usu.ac.id
Received: 07-Mar-2022
Revised: 23-Apr-2022
Accepted: 26-Apr-2022

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Cryptococcal meningitis is one of the most common opportunistic infections in immunocompromised patients. Mostly it manifests as subacute/chronic meningitis, although pathological findings suggest extensive tissue invasion of the brain parenchyma and meninges. This disease has a very high mortality rate, even with the administration of an antifungal combination.

CASE REPORT: Male, 53 years old, with clinical symptoms of headache, was experienced by the patient from 1 month before admission and worsening within 1 week. The headache describe throbbing throughout the head, with severe intensity, and does not go away with pain medications. The frequency of headaches is persistent and does not go away with pain medications. A history of weight loss was found, about 10 kg in 3 months. A history of free sex was found. History of HIV known since 1 day before admission to hospital and has not undergone antiretroviral treatment. The patient was diagnosed with cryptococcal meningitis on the basis of the finding of yeas t-like cells on the Indian ink test, and the patient was also a stage IV HIV patient with a decreased CD4 count. The patients treated with tapering off dexamethasone injection, 1× 960 mg Cotrimoxazole, 400 mg/24 h injection of fluconazole, and 3 × 1 folic acid, and received 1 × 1 fixed dose combination antiretrovirals therapy.

CONCLUSION: Cryptococcal meningitis is a disease caused by cryptococcal fungi and its incidence increases with the increase in diseases associated with immune system disorders such as HIV.

Introduction

Cryptococcosis is a fungal infection caused by the fungus Cryptococcus neoformans. This infection is widely found in the world and is generally experienced by patients with low immune systems, such as patients with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), patients on long-term corticosteroid treatment, organ transplantation, and lymphoreticular malignancies. Infection by Cryptococcus neoformans mainly causes meningitis and meningoencephalitis in people infected with HIV/AIDS diagnosed as cryptococcal meningitis [1].

Cryptococcal meningitis is known as the most common clinical manifestation and is the second most common opportunistic infection associated with AIDS in Africa and South Asia with a 15%– 30% incidence of cryptococcosis found in patients with AIDS. Without treatment with specific antifungals, mortality is reported to be 100% within two weeks of clinical presentation of cryptococcosis with meningoencephalitis in an HIV-infected population [1].

In Indonesia, it is estimated that the incidence of Cryptococcal infection ranges from 5 to 30%. The Department of Parasitology, Faculty of Medicine, University of Indonesia noted was significant increase the incidence of cryptococcal meningitis in HIV patients by 21.9%. According to data from the RSCM in 2004–2006, the mortality rate for cryptococcal meningitis was 45%, while in 2007–2010 it was 51.4% [2], [3].

The most common clinical manifestations of cryptococcal infection in the central nervous system (CNS) are headache, nausea, and fever, while less common manifestations include meningismus, confusion or altered mental status, seizures, visual disturbances, and other focal neurological deficits [4].

Cryptococcal meningitis is diagnosed clinically, laboratory, and serologically. Judging from the clinical manifestations, the suspicion toward cryptococcal increases in patients with a history of immunosuppression with complaints of severe headaches that are felt within a few weeks, neck stiffness, and accompanied by neurological symptoms such as changes in mental status [5]. Management of cryptococcal meningitis is divided into three stages, namely, induction, consolidation, and therapy maintenance [5], [6]. The goal of induction therapy is rapid sterilization of cerebrospinal fluid [6].

Case Report

A man, 53 years old, came with the complaint of headache. This has been experienced since ±

1 month before admission to the hospital and has worsened in this 1 week. Headache is throbbing throughout the head, with severe intensity. Headaches usually come on slowly, and do not go away with painkillers. Headache does not get worse when doing physical activity or coughing. The frequency of headaches is continuous; there is no extra influence or precipitating factor on the headache. History of cough found since 1 month. A history of weight loss was found, about 10 kg in these 3 months. Free sex habits found. Patient with a known history of HIV from 1 day before admission to the hospital and has not received antiretroviral treatment.

Neurological examination revealed compos mentis consciousness with nuchal rigidity. On laboratory investigations of blood, it was found that the results were reactive to the three methods of anti-HIV examination. There was also a decrease in the value of 4% CD by 2% and absolute CD4 by 10 cells/uL.

On examination of the cerebrospinal fluid, MN cells were 71.4% and PMN cells 28.6%, and the total protein was within normal limits, which was 12.00. In Indian ink staining, yeast like cells are found (Figure 1).

On a CT scan of the head with contrast, the patient concluded that the result was no visible bleeding, intracerebral SOL, or other intracranial abnormalities (Figure 2).

The patient received therapy in the form of dexamethasone injection 5 mg/6 h and reduced every 3 days by tapering off, paracetamol 3 × 1000 mg, cotrimoxazole 1 × 960 mg, fluconazole injection 400 mg/day for 2 weeks, and folic acid 1 × 1. The patient was also consulted to Infectious Tropical Diseases (PTI) section, and received FDC ARV therapy (Tenofovir, Lamivudine, and Evafirenc) once a day.

During the treatment period, the patient felt a decrease in headache, and the patient went home for outpatient treatment.

Case Discussion

Infections caused by cryptococcal fungi or known as cryptococcosis (cryptococcosis) are mycoses that are global in nature, occur throughout the world, and can cause death. This organism is an encapsulated fungus. This capsule is the most virulent factor. This species produces no toxins and causes little inflammation [7].

Cryptococcal meningitis in HIV is usually found when the CD4 cells are < 100 cells/ul. This disease is an indication of the initial diagnosis of HIV disease in 2% of patients. HIV/AIDS often causes cryptococcal meningitis so that this disease ranks second as the

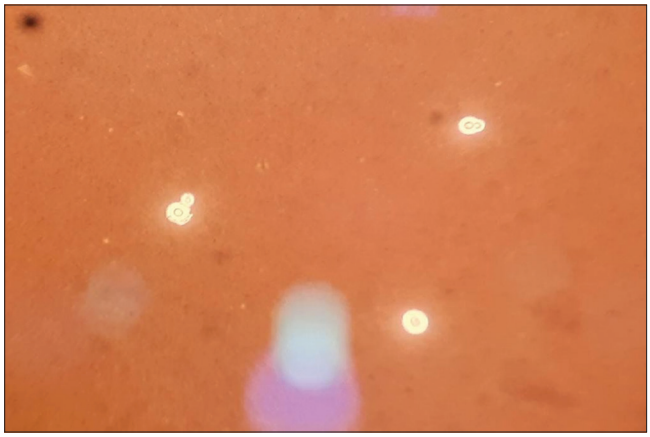

Figure 1: Indian ink coloring

cause of death in HIV patients after tuberculosis. Although highly active antiretroviral therapy (HAART) is widely available, cryptococcal meningitis is still a problem. Especially regarding appropriate combination antifungal therapy, duration of therapy, accurate indicators of response to therapy, management of increased intracranial pressure (ICP), and the use of adjunctive therapies such as corticosteroids and other anti-inflammatory drugs [8].

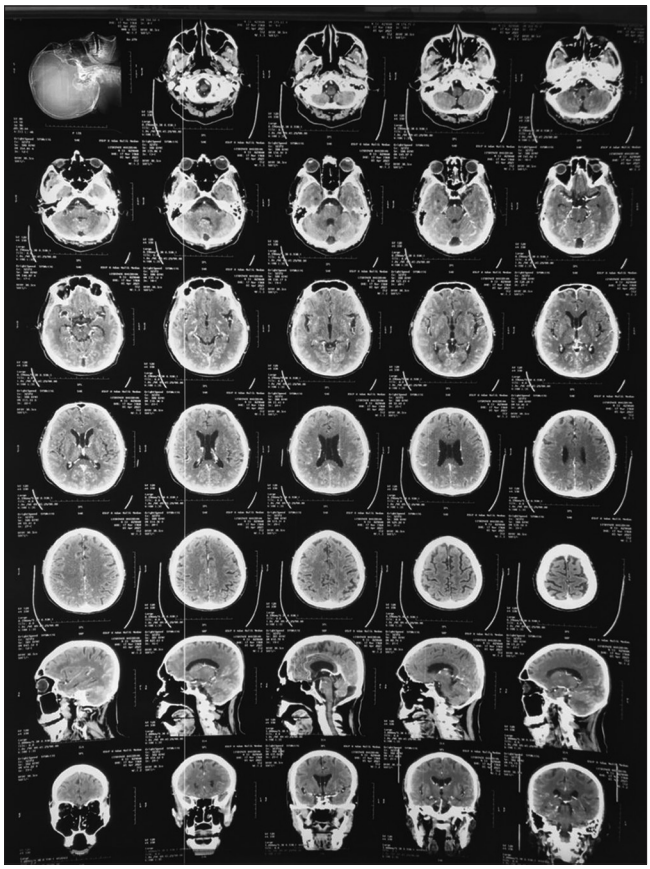

Figure 2: CT scan of the head with contrast of the patient, the conclusions were as follows: No bleeding, intracerebral SOL, or other intracranial abnormalities were seen

In this case report, the authors present a case report of cryptococcal meningitis in a 53-year-old who was treated at H. Adam Malik Hospital, Medan. The

diagnosis of cryptococcal meningitis in this patient was made based on several clinical manifestations supported by laboratory investigations and lumbar puncture. Establishing this diagnosis is in accordance with the previous theory that Cryptococcal meningitis is a central nervous system infection with subacute or chronic onset [2]. AIDS patients with cryptococcal meningitis are classified as clinical stage IV AIDS patients, which is the most severe clinical stage. Usually, these patients have CD4 (cluster of differentiation 4) values <100 cells/mm [3], [7].

On examination of the cerebrospinal fluid, MN cells were 71.4% and PMN cells were 28.6%, and the total protein was within normal limits, which were 12.00. In Indian ink staining, yeast like cells were found.

A lumbar puncture will usually show an increase in opening pressure. The definitive diagnosis for cryptococcal meningitis is the presence of the fungus in CSF or blood serologic examination. CSF usually shows a mild leukocytosis with a predominance of mononucleosis (50–500 cells/uL). CSF protein rarely exceeds 500–1000 mg/dL and may be normal especially in HIV patients. In HIV patients, the cell count is much lower [8].

Painting with Indian ink is very simple and relatively sensitive and can be used for quick diagnosis. Sensitivity can reach 75% when the material is centrifuged. However, if the concentration of the fungus is <10 colony-forming units (CFU), the examination with Indian ink is usually negative. In HIV patients, there is a high concentration of fungi in CSF so that painting with Indian ink will gave positive results [8], [9], [10].

On a CT scan of the head with contrast, the patient concluded the result was no bleeding, intracerebral SOL, or other intracranial abnormalities were seen. CT scan of the head appears normal in more than 50% of cases. No lesions were pathognomonic. Even if there are abnormalities, they are similar to tuberculous meningitis. The most common abnormality is hydrocephalus [8], [10].

On MRI of the head more often abnormalities shows. The abnormalities that appear depend on the accompanying disease. For example, in AIDS patients, diffuse cortical atrophy will appear and hydrocephalus is rare. Cortical atrophy in this patient may be a direct result of his retrovirus infection. In contrast, gyral enhancement is more common in non-HIV patients. Some patients present with focal, clustered, hyperintense lesions in the basal ganglia or midbrain. MRI repeats will show enhancement due to the inflammatory process [4], [8], [11].

The patient received therapy in the form of dexamethasone injection 5 mg/6 h and reduced every 3 days by tapering off, paracetamol 3 × 1000 mg, cotrimoxazole 1 × 960 mg, fluconazole injection 400 mg/day for 2 weeks, and folic acid 1 × 1. The patient was also consulted to Infectious Tropical Diseases (PTI) section and received FDC ARV therapy (Tenofovir, Lamivudine, and Evafirenc) once a day.

In cryptococcal meningitis, antifungal treatment is given in three stages: Induction, consolidation, and maintenance. The length of each stage is adjusted to the patient's condition. The induction stage may be extended if the patient remains in a coma, or worsens, does not change, or there is an increase in intracranial pressure. In this case, the induction stage can be extended for 1–6 weeks [12], [13].

According to the Infectious Diseases Society of America (IDSA) in 2010, the management of cryptococcal meningitis with HIV can be given induction therapy AmBD (0.7–1.0 mg/kg/day) + Flucytosine (100 mg/kg/day) for 2 weeks, liposomal AmB (3-4 mg/kg/day) or ABLC (5 mg/kg/day, if renal function is impaired) + Flucytosine (100 mg/kg/day) for 2 weeks, AmBD (0.7–1.0 mg/kg/day) or liposomal AmB (3-4 mg/kg/day) or ABLC (5 mg/kg/day, and for patients who cannot tolerate flucytosine) for 4–6 weeks. Consolidation therapy was given fluconazole (400 mg/day) for 8 weeks. Maintenance therapy is fluconazole (200 mg/day) for 1 year [8].

With regular treatment and screening for HIV patients on HAART, the mortality rate of patients with cryptococcal meningoencephalitis within 3 months of therapy is 20%. Meanwhile, in HIV patients with cryptococcal meningoencephalitis who did not receive antifungals, the mortality rate within 2 weeks was 100% [14].

Conclusion

Cryptococcal meningitis is a disease caused by the cryptococcal fungus and its incidence is increasing with the increase in diseases associated with immune system disorders such as HIV. Clinical symptoms range from focal neurological abnormalities to seizures and coma. Diagnosis is determined by the presence of fungi in cerebrospinal fluid and blood by staining, antigen serology and culture. Treatment is aimed at eradicating the fungus and treating complications. Management of complications includes treatment of increased intracranial pressure through lumbar puncture or installation of ventriculoperitoneal shunting.

References

1. Efrida E, Ekawati D. Cryptococcal meningitis: Clinical aspects and laboratory diagnosis. J Kesehatan Andalas. 2012;1(1):39-44.
2. Gunawan PY, Feliana F, Cucunawangsih C. Clinical Features and Analysis of Cerebrospinal Fluid in Cryptococcal Meningitis

Patients with or without Human Immunodeficiency Virus Infection at SHLV Hospital. Medicinus. 2015;4(8):247-53.

3. Indrati AR. Diagnosis laboratorium Pada Infeksi *Cryptococcus*; 2012. Available from: http://pustaka.unpad.ac.id/wpcontent/uploads/2015/08/Diagnosis-Laboratorium-pada- Infeksi-Cryptococcus.pdf. [Last accessed on 2021 Aug 25].
4. Duarte SB, Oshima MM, Mesquita JV, Nascimento FB, Azevedo PC, Reis F. Magnetic resonance imaging finding in central nervous system cryptococcosis: Comparison between immunocompetent and immunocompromised patients. Radiol Bras. 2017;50(6):359-65. https://doi.org/10.1590/0100-3984.2016.0017

   PMid:29307925
5. Utama MS, Sukmawati DD, Gayatri AA, Somia IK, dan Merati KT. Toksoplasmosis and Other Neurologic Infection; 2017. Available from: https://simdos.unud.ac.id/uploads/file_penelitian_dir/bf91cf0224e65c420ab4af3a622a5cc 3.pdf. [Last accessed on 2021 Aug 25].
6. Abassi M, Boulware DR, Rhein J. Cryptococcal meningitis: Diagnosis and management update. Curr Trop Med Rep. 2015;2(2):90-9. https://doi.org/10.1007/s40475-015-0046-y

   PMid:26279970
7. Perfect J, Dismukes W, Dromer F, Goldman D, Graybill J, Hamill R, *et al*. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious disease society of America. Clin Infect Dis. 2010;50(3):291-332.
8. Sugianto P. Meningitis kriptokokus. In: Sugianto P, Mawuntu A, editors. Infeksi Pada Sistem Saraf. 2nd ed. Surabaya: Pusat Penerbitan dan Percetakan Universitas Airlangga; 2019. p. 125-46.
9. Susarla K, Mahadevan A. *Cryptococcus*. In: Turgut M, Challa S, Akhaddar A, editor. Fungal Infections of the Central Nervous System. Switzerland: Springer; 2019. p. 167-80.
10. Loyse A, Wainwright H, Jarvis JN, Bicanic T, Rebe K, Meintjes G, *et al*. Histopathology of the arachnoid granulations and brain in HIV-associated crypto-coccal meningitis: Correlation with cerebrospinal fluid pressure. AIDS. 2010;24(3):405-10. https://doi.org/10.1097/QAD.0b013e328333c005

    PMid:19952714
11. Tan ZR, Long XY, Li GL, Zhou JX, Long L. Spectrum of neuroimaging findings in cryptococcal meningitis in immunocompetent patients in China a series of 18 cases. J Neurol Sci. 2016;368:132-7. https://doi.org/10.1016/j.jns.2016.06.069

    PMid:27538616
12. Imran D, Estiasari R, dan Maharani K. Infeksi Oportunistik Susunan Saraf Pusat pada AIDS. In: Aninditha T, Wiratman W, editors. Buku Ajar Neurologi. Buku 1. Deparetmen Neurologi Fakultas Kedokteran Universitas Indonesia; 2017. p. 239-48.
13. Day JN, Chau TT, Wolbers M, Mai PP, Dung NT, Mai NH, *et al*. Combination antifungal thera- py for cryptococcal meningitis. N Engl J Med. 2013;368(14):1291-302. https://doi.org/10.1056/NEJMoa1110404

    PMid:23550668
14. French N, Gray K, Watera C, Nakiyingi J, Lugada E, Moore M, *et al*. Cryptococcal infection in a cohort of HIV-1-infected Ugandan adults. AIDS. 2002;16(7):1031-8. https://doi.org/10.1097/00002030-200205030-00009

    PMid:11953469