

Case Report

Disseminated cryptococcal infection diagnosed on autopsy in a human immunodeficiency virus-positive patient – A rare case report with review of literature

Babita Rani,¹ Shilp Rani², Arpita Kumar²¹Department of Pathology, Government Medical College, Patiala, ²Department of Pathology, Adesh Medical College, Bathinda, Punjab, India.***Corresponding author:**

Babita Rani,
Department of Pathology,
Government Medical College,
Patiala, Punjab, India.

docbabgarg05@gmail.com

Received: 03 July 2025
Accepted: 14 September 2025
Epub Ahead of Print: 17 February 2026
Published:

DOI
10.25259/AUJMSR_73_2025

Quick Response Code:**ABSTRACT**

Cryptococcus neoformans is a ubiquitous yeast like fungus that causes opportunistic infection in immunocompromised individuals. Objective of this case report is to study the histopathological findings in various organs in a case of disseminated Cryptococcal infection diagnosed on autopsy involving Kidney, Liver, Spleen, Lungs and Brain in human immunodeficiency virus (HIV) infected patient. Detailed postmortem gross and histopathological assessment of various organs was done to find out the cause of death. Patient was a known case of HIV infection and presented to the emergency with complaints of headache and chest pain. History of altered sensorium was also present. Histopathological examination along with the help of special stains, made the diagnosis of disseminated Cryptococcal infection.

Keywords: Autopsy, Disseminated *Cryptococcus*, Histopathology, Human immunodeficiency virus

INTRODUCTION

Cryptococcus is a yeast, round to oval in shape, with a large polysaccharide capsule ranging from 1 to 30 μ m. There are four capsular types A, B, C, and D. Weathered pigeon droppings commonly contain serotypes A or D (*Cryptococcus neoformans*). *C. neoformans* is a ubiquitous yeast-like fungus that causes opportunistic infection in immunocompromised individuals (human immunodeficiency virus/acquired immunodeficiency syndrome [HIV/AIDS], chronic hypogammaglobulinemia, and organ transplant recipients).^[1] Infection is contracted through inhalation (soil and pigeon droppings), as it is isolated from the nasopharynx of 50% of AIDS patients with cryptococcosis.^[2,3] Incubation period is variable, with a median duration of 2 weeks in HIV positive patients. Mortality rates can reach 30–50% even with antifungal therapy. Of the survivors, 40% suffer from severe neurological conditions such as hydrocephalus, cranial nerve palsies, diminished mental function, and vision loss. Relapse occurs in 25% of these patients.^[4]

India has seen a sharp rise in the prevalence of cryptococcal meningitis over the past 20 years. For 60–70% of people with HIV, cryptococcosis is the condition that defines AIDS. The prevalence of cryptococcosis in HIV/AIDS patients is reported to be 1.7–4.7% in India,^[5,6] and its incidence in immunocompetent individuals is also on the rise, making it imperative to study the pathological findings to improve its current management. However, current literature shows a limited number of autopsy studies on cryptococcal infection.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, transform, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

©2026 Published by Scientific Scholar on behalf of Adesh University Journal of Medical Sciences & Research

We present a case of disseminated cryptococcosis in an HIV-positive patient that evaded clinical recognition, and the final diagnosis was established on autopsy.

CASE REPORT

A 35-year-old male presented to the emergency with complaints of chest pain, cough, and headache for 20 days. The patient was a known case of HIV for 5 years and had defaulted on antiretroviral therapy. No other medical record was available as the patient was under trial, in judicial custody. There was a history of 12 kg weight loss over a period of 2 months, along with signs of muscle wasting. On examination, signs of dehydration and altered sensorium were noted, but signs of meningeal irritation were absent. The temperature was 99. F and other vitals were within normal limits. Routine examinations revealed pancytopenia with a total leukocyte count of $4,000/\mu\text{L}$ and absolute lymphocyte count of $800/\mu\text{L}$. The CD4 count was reported as $200/\mu\text{L}$. Non-contrast head computed tomography head revealed a small hypodense area in the right external capsule, suggestive of a likely subacute/chronic infarct. However, the patient expired before any further medical intervention. Autopsy was done, and the viscera were received in the pathology department in 10% neutral-buffered formalin. Gross examination and sampling of organs were performed, including part of the brain, lungs, liver, kidneys, spleen, and heart. Postmortem examination revealed a foul-smelling yellow colored discharge covering the meninges. Cut section showed a soap bubble appearance with numerous variably sized cysts, both in the cortical and subcortical areas. Both lungs were heavy, edematous, and hemorrhagic. The rest of the viscera also showed features of edema and congestion. Microscopic examination of sections taken from the brain revealed numerous cryptococcal yeast forms (both extracellular and intracellular) infiltrating the meninges and brain parenchyma along with sheets of macrophages [Figure 1a]. The yeasts showed narrow-based budding and were pleomorphic. The rest of the brain parenchyma showed features of congestion and edema. Histopathological findings were consistent with cryptococcal meningoencephalitis. Microscopic examination of sections examined from both kidneys, lungs, liver, and spleen showed infiltration by numerous yeast forms consistent with the morphology of *Cryptococcus* [Figure 1 b and c] along with lymphocytic infiltration suggestive of a pauci-reactive pattern. Occasional multinucleated giant cells were seen in the lung parenchyma, but no well-defined granulomas were seen. No necrosis or abscess formation was seen. Special stain periodic acid-Schiff (PAS) stain was used to highlight the thick polysaccharide capsule of yeast forms [Figure 1 d]. Multiple sections examined from the remaining viscera, including heart and coronaries, were unremarkable. Histopathological examination findings were consistent with disseminated cryptococcal infection.

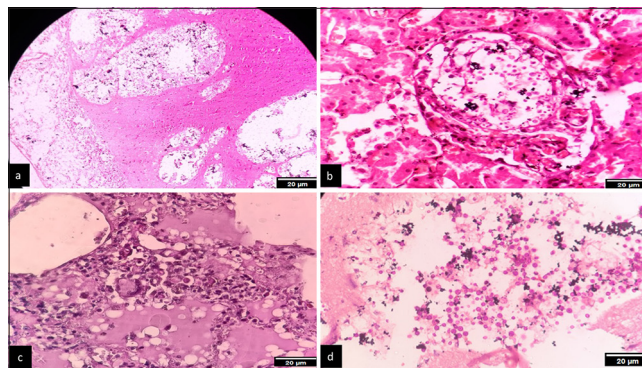


Figure 1: (a) Soap bubble appearance in brain (H and E, 100x). (b) Cryptococcal yeast forms in glomerulus of kidney (H and E, 400x), (c) Microphotograph showing fungal yeast forms in lung along with multinucleated giant cell (H and E, 400X). (d) Fungal yeast forms in the brain (PAS, 400x). H and E: Hematoxylin and Eosin stain. PAS: Periodic acid-schiff stain.

DISCUSSION

In this case report, the patient presented with headache and altered sensorium without any other signs of meningeal irritation. Radiological findings were more inclined toward an infarct, evidence for cryptococcal meningitis was not definitive. Overall, only 20% cases show a neurological finding on imaging, and focal neurological deficits or seizures are seen in 20% of cases. Although in our case lumbar puncture was not done, cerebrospinal fluid examination and India Ink preparation can be used for identification of cryptococcosis, as it is positive in 74–88% of cases.^[7]

Serum cryptococcal antigen followed by culture is the most sensitive method to diagnose cryptococcosis, especially in HIV infected individuals with CD4 count $<100 \text{ cells}/\mu\text{L}$. It can be added as a screening tool to detect cryptococcal antigenemia that precedes the development of overt symptoms.^[8] This test is currently not commonly available in our country and may also test false negatives if hematogenous spread has not occurred.

Immunosuppression is the strongest risk factor for disease development. Out of the global 1 million cases of AIDS related cryptococcosis, 6% cases have a CD4 count $<100 \text{ cells}/\mu\text{L}$.^[9] Patients with a median CD4 cell count of $<50 \text{ cells}/\mu\text{L}$ and an advanced immunosuppressive stage are typically the ones who present with cryptococcal meningitis. In our case, CD4 count was $100 \text{ cells}/\mu\text{L}$. No other coexisting infection, such as tuberculosis or candidiasis, was present in our case but is strongly associated with a CD4 count of $<200 \text{ cell}/\mu\text{L}$.^[10]

Histopathological examination helps in assessing the extent of immunological response, such as in this case report, the presence of multinucleated giant cells in sections examined from the lung indicates some degree of immunological response, but well-formed granulomas

were absent as would be seen in an immunocompetent patient.^[11,12] As per Schwartz classification,^[13] this response can be divided into two patterns, reactive and paucireactive. In the reactive pattern, well-defined granulomas consisting of multinucleated giant cells, macrophages, and lymphocytes are seen, whereas in the latter, extracellular yeast forms with minimal inflammatory response are seen. In this case report, histopathological findings were suggestive of a paucireactive pattern due to a lack of well-defined granulomas, although both extracellular and intracellular PAS-positive yeast forms were seen. Other histochemical stains such as Mayer's Mucicarmine and Fontana Masson can be used to stain the capsule magenta and fungal melanin brown, respectively. Dissemination in the kidneys, liver, and spleen was noted, which can be due to immunosuppression and defects in T-cell function. In an immunocompetent individual, primary lung infection would present as a circumscribed nodular intra-alveolar proliferation of cryptococci with reactive histiocytes. However, neutrophils are not seen in both immunocompromised and immunocompetent individuals.

Extensive involvement of brain parenchyma and meninges in the form of multiple cystic lesions containing encapsulated yeasts, both in cortical and subcortical regions, was consistent with the pathological findings of cryptococcal meningitis in HIV/AIDS.^[14,15]

Early diagnosis and antifungal therapy consisting of fluconazole and amphotericin B can help in the resolution of symptoms, but in some cases, relapse or treatment failure can occur, thus making autopsy the gold standard for estimating disease extent in such challenging cases.

Thus, patient's poor outcome can be mainly attributed to nonspecific clinical findings, lack of clinical diagnosis, the fulminant nature of the disease, the immunocompromised status of the patient, and non-adherence to anti-retroviral therapy. Limited access to medical care and poor living conditions can also be contributed factors.

CONCLUSION

Cryptococcal infection is the most prevalent opportunistic fungal infection found in HIV patients. Despite particular therapy, mortality from cryptococemia remains high, due to lack of routine screening and delayed diagnosis. In this case report, diagnosis and dissemination of cryptococcosis were done on autopsy. Clinicians can play a major role by requesting more autopsies in cases of unexpected death in HIV patients, as there are a limited number of case reports on cryptococcosis. Histopathological evaluation of such cases is important to determine the pathogenesis and immunological behavior of *Cryptococcus* so that further research can be done to treat such cases for better clinical outcomes. More studies

are required to further explicate morphological findings associated with disseminated cryptococcal infection, and autopsy provides a definitive diagnosis in challenging cases.

Ethical approval: Institutional Review Board approval is not required.

Declaration of patient consent: Patient's consent not required as patients identity is not disclosed or compromised.

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Aberg JA, Powderly WG. Cryptococcosis. *Adv Pharmacol* 1997;37:215-51.
2. Sukroongreung S, Eampokalap B, Tansuphaswadikul S, Nilakul C, Tantimavanich S. Recovery of *Cryptococcus neoformans* from the nasopharynx of AIDS patients. *Mycopathologia* 1998;143:131-4.
3. Shanthi B, Kannan I. A case of cryptococcal meningitis in HIV positive patient in a tertiary care hospital in Kancheepuram district, Tamilnadu, India. *Int J Med Res Rev* 2015;3:250-3.
4. Jain N, Wicks BL, Keller SM, Fu J, Kesadevall A, Jain P, et al. Molecular epidemiology of clinical *Cryptococcus neoformans* strains from India. *J Clin Microbiol* 2005;43:5733-42.
5. Mirza SA, Phelan M, Rimland D, Graviss E, Hamil R, Brandt ME, et al. The changing epidemiology of cryptococcosis: An update from population-based active surveillance in 2 large metropolitan areas, 1992-2000. *Clin Infect Dis* 2003;36:789-94.
6. Chowdhary A, Randhawa HS, Prakash A, Meis JF. Environmental prevalence of *Cryptococcus neoformans* and *Cryptococcus gattii* in India: An update. *Crit Rev Microbiol* 2011;38:1-16.
7. Rajasingham R, Govender NP, Jordan A, Loyse A, Shroufi A, Denning DW, et al. The global burden of HIV-associated cryptococcal infection in adults in 2020: A modelling analysis. *Lancet Infect Dis* 2022;22:1748-55.
8. Jarvis JN, Lawn SD, Vogt M, Bangani N, Wood R, Harrison TS. Screening for cryptococcal antigenemia in patients accessing an antiretroviral treatment program in South Africa. *Clin Infect Dis* 2009;48:856-62.
9. Gazzoni AF, Severo CB, Salles EF, Severo LC. Histopathology, serology and cultures in the diagnosis of cryptococcosis. *Rev Inst Med Trop Sao Paulo* 2009;51:255-9.
10. 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;7:1031-8.
11. Pandit L, Agrawal A, Shenoy S, Kamath G. Cryptococcal meningitis and pulmonary cryptococcosis in a non-HIV infected patient. *Eur J Gen Med* 2006;3:80-2.
12. Akakpo KP, Quayson SE, Lartey M. Disseminated cryptococcosis in a patient with HIV/AIDS at a teaching hospital in Ghana. *SAGE Open Med Case Rep* 2015;3:2050313X14565421.

13. Akrim Y, Ouasif H, Zrikem H, El Hakkouni A. Disseminated cryptococcosis revealing an HIV infection: A case report. *Cureus* 2023;15:e37403.
14. Schwartz DA. Characterization of the biological activity of *Cryptococcus* infections in surgical pathology. The budding index and carminophilic index. *Ann Clin Lab Sci* 1988;18:388-97.
15. Martin-Blondel G, Ysebaert L. Images in clinical medicine. Disseminated cryptococcosis. *N Engl J Med* 2014;370:1741.

How to cite this article: Rani B, Rani S, Kumar A. Disseminated cryptococcal infection diagnosed on autopsy in a human immunodeficiency virus-positive patient – A rare case report with review of literature. *Adesh Univ J Med Sci Res*. doi: 10.25259/AUJMSR_73_2025