Clinical Case Reports

Open Access

CASE REPORT

# Pulmonary cryptococcosis presenting as acute severe respiratory distress in a newly diagnosed HIV patient in Tanzania: a case report

Daniel W. Gunda[1], Fatma A. Bakshi[1], Peter Rambau[2] & Semvua B. Kilonzo[1]

[1]Department of Internal Medicine, Bugando Medical Centre, Catholic University of Health and Allied Science, P. O BOX 1464, Mwanza, Tanzania
[2]Department of Pathology, Bugando Medical Centre, Catholic University of Health and Allied Sciences, P. O BOX 1464, Mwanza, Tanzania

**Correspondence**
Semvua B. Kilonzo, Department of Internal Medicine, Catholic University of Health and Allied Science, Bugando Medical Centre, P. O BOX 1464, Mwanza, Tanzania. Tel: +255 756 590665; Fax: +255 028 2502678; E-mail: sekipcb@yahoo.com

**Funding Information**
We thank the staff members of the Department of Internal Medicine of Bugando Medical Centre for their support.

Received: 10 April 2015; Revised: 25 May 2015; Accepted: 2 July 2015

***Clinical Case Reports*** **2015; 3(9): 749–752**

doi: 10.1002/ccr3.337

### Key Clinical Message

Pulmonary cryptococcosis is a common condition in HIV-infected patients which is frequently missed or misdiagnosed in resource-limited countries. We report a case of HIV/AIDS patient who was misdiagnosed with a fatal outcome. There is a need to implement screening tools to be used where the diagnosis may not be confirmed.

### Keywords

Pulmonary Cryptococcus HIV Tanzania.

## Introduction

Pulmonary cryptococcosis (PCr) is a common condition in HIV/AIDS patients with acute respiratory symptoms, second to pulmonary tuberculosis (PTB) [1, 2]. Cryptococcosis is caused by the fungi *Cryptococcus neoformans* and *Cryptococcus gattii* which are widely distributed in nature [3]. The organism is usually acquired through inhalation of spores or dried yeast cells from the environment and is usually deposited in the alveoli where it may be contained. In patients who are immune-compromised, a localized infection may occur and progress into a life-threatening pneumonia with acute respiratory failure [4, 5] or else it enters the blood stream to cause a more disseminated form of infection which commonly presents as cryptococcal meningitis (CM) [6].

Manifestations of PCr in immune-compromised hosts are quite variable; seldom subclinical, to severe condition with substantial mortality [7]. In symptomatic patients, the clinical features are nonspecific and can simulate a wide range of other respiratory distress diseases [8, 9] hence frequently misdiagnosed as pulmonary tuberculosis, *Pneumocystis carinii* Pneumonia (PCP), or severe bacterial pneumonia in the background of immune suppression [10, 11]. The commonly presenting features of PCr include fever, cough, dyspnea, pleuritic chest pain, hemoptysis, tachypnea, hypoxia, crepitations on auscultation, and diffuse interstitial infiltrates on chest radiography [2, 3, 7, 12, 13].

A definitive diagnosis of PCr requires identification of the organism by culture or India ink staining of samples obtained by bronchoalveolar lavage (BAL) or tissue biopsy [3, 8, 9, 14]. Tanzania like most of other resource-limited countries face a diagnostic limitation for this condition and most of these cases are presumed to be frequently missed or misdiagnosed. We report a case of a newly diagnosed HIV/AIDS middle aged male who presented with acute respiratory distress secondary to PCr which was initially misdiagnosed as PCP with fatal outcome.

## Case Presentation

A 33-year-old male presented with a 1-week history of acute onset of difficulty in breathing, right-sided pleuritic chest pain with intermittent low-grade fever. Physical

examination revealed an obese middle-aged man in severe respiratory distress using accessory muscles of respiration, tachypnoeic (RR 38 bpm), and severely hypoxic with $SPO_2$ of 78% in room air. He was not cyanosed. His respiratory examination was significant for presence of diffuse course crackles bilaterally. He had a BP of 110/70 mmHg and PR 110 beats/min. The rest of physical examination was unremarkable. His chest X-ray showed diffuse alveolar and interstitial infiltrates bilaterally and the initial laboratory investigations were significant for Positive HIV antibodies. A provisional diagnosis of severe pneumonia due to *Pneumocystis carinii* infection was entertained with differential diagnoses of severe bacterial pneumonia and pulmonary tuberculosis. On the emergency basis, he was managed as per our standard treatment protocols in the ICU [15] with 10 L of Oxygen, cotrimoxazole 1920 mg per oral q8hourly along with prednisolone 40 mgs per oral q12 hourly for probable PCP infection. He was also given intravenous ceftriaxone 1 g q 12hourly in combination with azithromycin 500 mg per oral q 12hourly for coverage of both typical and atypical bacteria. The patient rapidly deteriorated that and in spite of all the efforts he died just 10 h after admission. A consent was obtained for autopsy which was only limited to the chest. The gross histopathologic examination of the lungs revealed heavily congested lungs oozing blood-stained fluid with hyperemic and frothy small airways (Fig. 1). On microscopic examination of the tissue sections, interstitial edema which was mixed with hemorrhage with few lymphocytic infiltrates was seen. There was also presence of desquamated cells in the alveoli. Several round organisms with a thick capsule in the interstitial and alveoli together with foreign body giant cells were seen in some areas (Fig. 2). Periodic acid Schiff (PAS) staining was positive, and very thick capsulated organisms were highlighted (Fig. 3). According to our pathologist, these findings are consistent with pulmonary cryptococcosis. However, we did not see any hyaline membrane or foamy amorphous material-containing cell debris which is typical for PCP infection. The silver stain was not available in our settings. No acid-fast bacilli (AFB) which were detected on the Ziehl– Nielsen stain. A serum result which was traced later was positive for cryptococcal antigen.

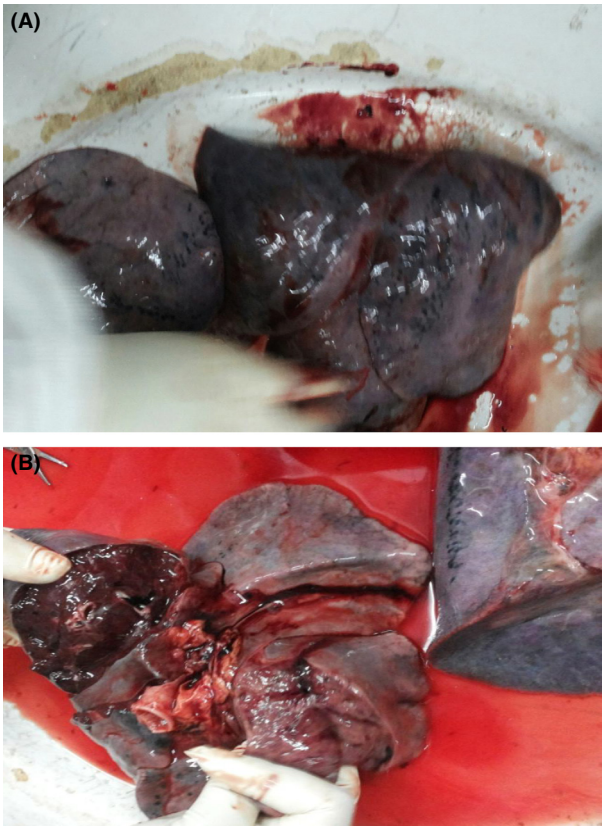


**Figure 1.** Gross appearance of the lungs after dissection of the chest. (A) Dark reddish lungs with loss of normal color of the lungs. (B) Hemorrhagic congested lungs on cut surface.

## Discussion

Pulmonary Cryptococcus in HIV/AIDS population is common in sub-Saharan Africa countries with high mortality [2, 16]. In Tanzania, the magnitude of PCr is unknown. Cryptococcal meningitis (CM), which on clinical grounds is a late stage of the disease has been extensively studied and documented with a significant high prevalence and mortality in the country [17, 18].

Prior to the presentation of meningeal symptoms, the majority of the patients with CM usually present with unspecific features of respiratory distress [26] which is usually misdiagnosed and mistreated. Autopsy studies in Uganda and South Africa has shown a very high rate of PCr misdiagnosis. More than 95% of the patients with PCr were misdiagnosed [2] [16] and among them more than 50% were treated for PTB. Comparable to these studies, our patient presented with acute onset of severe respiratory distress symptoms and was misdiagnosed as PCP, and we as well did not suspect PCr before autopsy. In this outlook, therefore a timely diagnosis and treatment of these patients at a primary lung involvement would likely improve their outcome [23, 24] as the capability to optimally execute the complicated management of CM which is also inadequate in a resource-limited setting like ours [6, 19–22].

Bronchoalveolar lavage (BAL) and tissue biopsy which are the gold standard diagnostic investigations are usually not routinely available in most of the resource-limited settings like ours, and clinical-radiological presentation of PCr is very unspecific which poses a big diagnostic

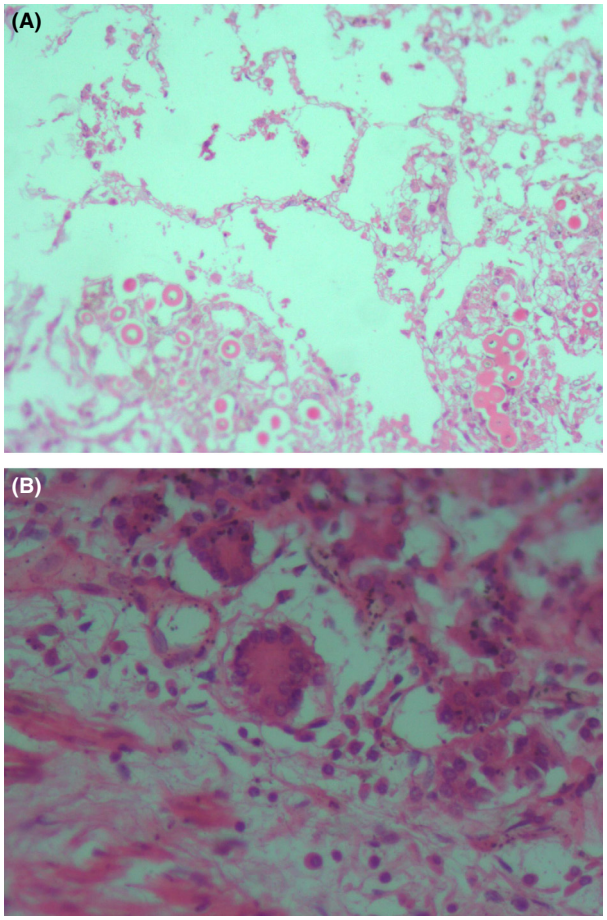


**Figure 2.** H&E histological stain showing (A) interstitial edema, desquamated cells in alveoli and round fungal organism with a thick capsule. (B) Giant cells, few lymphocytes and fungal organism in the interstitial.

challenge. In light of this information, we assume that many cases of PCr are missed in Tanzania and therefore not reported. Consequently, serum cryptococcal antigen (SCrAg) test, though nonspecific, may assist in the diagnosis of PCr. Majority of HIV/AIDS patients, who presents with respiratory symptoms and positive SCrAg, has also been found to have PCr [1, 25]. It is therefore important to perform SCrAg in HIV-infected patients presenting with respiratory.

Fluconazole remains the mainstay of treatment of PCr in a capacity where Amphotericin B is either not available or cannot be used safely. According to the available guidelines, severe PCr should be treated with a high dose of fluconazole 1200 mg once daily orally or intravenously for 14 days (induction phase), then 600–800 mg once daily orally for 8 weeks (consolidation phase) then 200 mg orally once daily for 6–12 weeks as a maintenance phase [27, 28]. In milder cases, a lower dose of Fluconazole

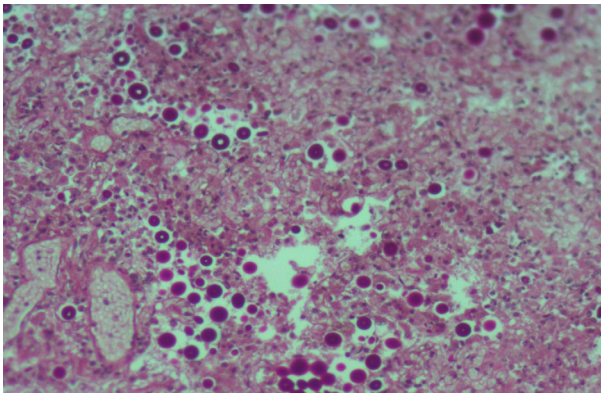

**Figure 3.** Periodic acid Schiff-stained histological section showing a well pink-stained capsule.

400 mg once daily orally 6–12 months is recommended. Lumber puncture should be performed before commencement of the treatment to exclude meningeal involvement as may additionally require intracranial pressure management. An effective treatment is usually marked by resolution of PCr clinical symptoms, radiological normalization and negative test for Cryptococcal organisms [27]. From these recommendations, it is clear that our patient would benefit from antifungals (fluconazole), which is widely available in our facility only if the diagnosis was timely made.

## Conclusion and Recommendation

This case emphasizes the need to increase index of suspicion of PCr in all HIV/AIDS patients who present with respiratory symptoms among the clinicians. Obtaining a tissue or BAL for fungal culture is difficult in a resource-limited setting like ours, so empirical treatment to suspected cases should be provided to improve the outcome. Serum cryptococcal antigen (SCrAg) test should be available in all health facilities and advocated to the suspected cases to increase the window of confidence in areas where the microbiological tests cannot be performed. SCrAg is usually positive in essentially all patients with PCr [13]. Further studies are recommended to establish the magnitude and associated factors of this condition in Tanzania.

## Acknowledgment

We thank the staff members of the Department of Internal Medicine of Bugando Medical Centre for their support.

## Conflict of Interest

Authors declare that they have no competing interests.

## Consent

Written informed consent was obtained from the patient's next-of-kin for publication of this case report and any accompanying images. The WBUCHS/BMC ethics review board provided the approval to publish this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

### References


1. Harris, J. R., M. D. Lindsley, S. Henchaichon, N. Poonwan, S. Naorat, P. Prapasiri, et al. 2012. High prevalence of cryptococcal infection among HIV-infected patients hospitalized with pneumonia in Thailand. Clin. Infect. Dis. 54:e43–e50.
2. Deok-jong Yoo, S., W. Worodria, J. L. Davis, A. Cattamanchi, S. den Boon, and R. Kyeyune, et al. 2010. The prevalence and clinical course of HIV-associated pulmonary cryptococcosis in Uganda. J. Acquir. Immune Defic. Syndr. 54:269–274.
3. Wasser, L., and W. Talavera. 1987. Pulmonary cryptococcosis in AIDS. Chest 92:692–695.
4. Velagapudi, R., Y. P. Hsueh, S. Geunes-Boyer, J. R. Wright, and J. Heitman. 2009. Spores as infectious propagules of *Cryptococcus neoformans*. Infect. Immun. 77:4345–4355.
5. Botts, M. R., and C. M. Hull. 2010. Dueling in the lung: how Cryptococcus spores race the host for survival. Curr. Opin. Microbiol. 13:437–442.
6. Jarvis, J. N., and T. S. Harrison. 2007. HIV-associated cryptococcal meningitis. AIDS 21:2119–2129.
7. Peng, Y., R. Ouyang, and Y. Jiang. 2014. Clinical characteristics of primary pulmonary cryptococcosis in 28 patients. Zhong Nan Da Xue Xue Bao Yi Xue Ban 39:49–55.
8. Tokman, S., and L. Huang. 2013. Evaluation of respiratory disease. Clin. Chest Med. 34:191–204.
9. Antinori, S. 2013. New insights into HIV/AIDS-associated cryptococcosis. ISRN AIDS 2013:471363.
10. Hu, H. J., P. Zhou, J. B. Hu, L. P. Deng, S. Z. Zhang, and K. J. Ying. 2006. A report of 12 cases of primary pulmonary cryptococcosis. Zhonghua Nei Ke Za Zhi 45:721–724.
11. Shirley, R. M., and J. W. Baddley. 2009. Cryptococcal lung disease. Curr. Opin. Pulm. Med. 15:254–260.
12. Batungwanayo, J., H. Taelman, J. Bogaerts, S. Allen, S. Lucas, A. Kagame, et al. 1994. Pulmonary cryptococcosis associated with HIV-1 infection in Rwanda: a retrospective study of 37 cases. AIDS 8:1271–1276.
13. Meyohas, M. C., P. Roux, D. Bollens, C. Chouaid, W. Rozenbaum, J. L. Meynard, et al. 1995. Pulmonary cryptococcosis: localized and disseminated infections in 27 patients with AIDS. Clin. Infect. Dis. 21:628–633.
14. Jarvis, J. N., and T. S. Harrison. 2008. Pulmonary cryptococcosis. Semin. Respir. Crit. Care Med. 29:141–150.
15. Department of Internal Medicine, B.M.C., Mwanza, Treatment Guideline for in patients Department 2012, Bugando Teaching Hospital Mwanza. unpublished
16. Wong, M. L., P. Back, G. Candy, G. Nelson, and J. Murray. 2007. Cryptococcal pneumonia in African miners at autopsy. Int. J. Tuberc. Lung Dis. 11:528–533.
17. Wajanga, B. M., S. Kalluvya, J. A. Downs, W. D. Johnson, D. W. Fitzgerald, and R. N. Peck. 2011. Universal screening of Tanzanian HIV-infected adult inpatients with the serum cryptococcal antigen to improve diagnosis and reduce mortality: an operational study. J. Int. AIDS Soc. 14:48.
18. Matee, M. I., and R. Matre. 2001. Pathogenic isolates in meningitis patients in Dar Es Salaam, Tanzania. East Afr. Med. J. 78:458–460.
19. Hamill, R. J., M. Bauer, M. A. Leal, S. G. Evans, P. D. Holtom, and D. A. Diamond. 2006. Free fluconazole for cryptococcal meningitis: too little of a good thing? Clin. Infect. Dis. 43:1074–1076.
20. Robinson, P. A., M. Bauer, M. A. Leal, S. G. Evans, P. D. Holtom, D. A. Diamond, et al. 1999. Early mycological treatment failure in AIDS-associated cryptococcal meningitis. Clin. Infect. Dis. 28:82–92.
21. Imwidthaya, P., and N. Poungvarin. 2000. Cryptococcosis in AIDS. Postgrad. Med. J. 76:85–88.
22. Bicanic, T., R. Wood, L. G. Bekker, M. Darder, G. Meintjes, and T. S. Harrison. 2005. Antiretroviral roll-out, antifungal roll-back: access to treatment for cryptococcal meningitis. Lancet. Infect. Dis 5:530–531.
23. Saag, M. S., R. J. Graybill, R. A. Larsen, P. G. Pappas, J. R. Perfect, and W. G. Powderly, et al. 2000. Practice guidelines for the management of cryptococcal disease. Infectious Diseases Society of America. Clin. Infect. Dis. 30:710–718.
24. Panigrahi, M. K., N. N. Kumar, V. Jaganathan, and S. V. Kumar. 2014. Pulmonary cryptococcosis with cryptococcal meningitis in an immunocompetent host. Lung India 31:152–154.
25. Visnegarwala, F., E. A. Graviss, C. E. Lacke, A. T. Dural, P. C. Johnson, R. L. Atmar, et al. 1998. Acute respiratory failure associated with cryptococcosis in patients with AIDS: analysis of predictive factors. Clin. Infect. Dis. 27:1231–1237.
26. Driver, J. A., C. A. Saunders, B. Heinze-Lacey, and A. M. Sugar. 1995. Cryptococcal pneumonia in AIDS: is cryptococcal meningitis preceded by clinically recognizable pneumonia? J. Acquir. Immune Defic. Syndr. Hum. Retrovirol. 9:168–171.
27. Perfect, J. R., W. E. Dismukes, F. Dromer, D. L. Goldman, J. R. Graybill, and R. J. Hamill, et al. 2007. Low CD4 count plus coma predicts cryptococcal meningitis in Tanzania. BMC Infect. Dis. 7:39.
28. Sloan, D. J., and V. Parris. 2014. Cryptococcal meningitis: epidemiology and therapeutic options. Clin. Epidemiol. 6:169–182.