

CASE REPORT

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# A rare case of disseminated pulmonary cryptococcosis in an immunocompetent patient

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## Abstract

Pulmonary cryptococcosis is an uncommon invasive fungal infection of the lungs seen in immunocompromised individuals but increasingly reported among the immunocompetent. We report a rare case of pulmonary cryptococcosis in an immunocompetent host highlighting its unique clinical and radiological presentation.

**Clinical trial number:** Not applicable.

**Keywords** Cryptococcus, Immunocompetent, Immunosuppressed, Dissemination, Pulmonary

## Background

Cryptococcosis is an opportunistic invasive systemic fungal infection predominantly diagnosed in immunocompromised individuals such as those with Acquired Immunodeficiency Syndrome (AIDS), hematological/lymphoproliferative malignancies and patients on immunosuppressive therapy e.g. post-transplant cases. Other at-risk individuals are patients with uncontrolled diabetes and cancer patients on chemotherapy. The infection is however being increasingly diagnosed among immunocompetent individuals; usually with a varied clinical and radiological presentation making diagnosis difficult in the majority of cases [1, 2].

Although transmission of the infection is via inhalation of cryptococcal spores making the lungs the primary site of infection, dissemination to other parts of the body such as the meninges, brain, skin and lymph nodes commonly occurs, often with clinically silent or no obvious pulmonary lesions in the immunosuppressed host [3]. Spread to the meninges is most predominant, making cryptococcal meningitis the commonest clinical form of the infection in the immunocompromised [4]. However, among immunocompetent individuals, isolated pulmonary infection tends to be more prevalent and this is known as pulmonary cryptococcosis (PC). Dissemination to other sites in the body could still occur in the immunocompetent individual when the disease is advanced [1, 5]. In a study by Zhang Y et al., more than half of the PC cases diagnosed were in apparently immunocompetent hosts [6]. Similarly, several other studies have demonstrated the high occurrence of the disease among immunocompetent individuals compared to immunocompromised patients [7, 8]. Although there have been few documented cases of PC among HIV-positive patients in sub-Saharan Africa, there has been no report of the disease among immunocompetent individuals in

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**Fig. 1** Frontal chest radiography showing complete opacification of the left lung with mediastinal shift to the right side

the sub-region as well as in Ghana [9, 10]. We therefore present this unique case of PC in an immunocompetent patient, highlighting the clinical and radiological characteristics of the disease as well as the diagnostic challenges faced, with the aim of creating awareness.

### Case presentation

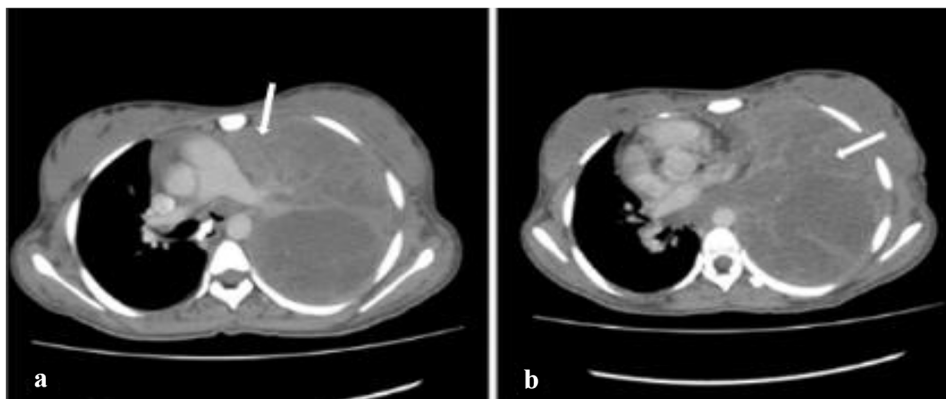
A 19-year-old young female was referred to the TB clinic of a tertiary hospital with about 3 weeks history of shortness of breath and a total left “whiteout” on a chest radiograph suspected to be a massive left pleural effusion (Fig. 1). She had a 5-month history of cough, productive of scanty clear sputum with associated night sweats and minimal weight loss. A chest tube was passed at a district hospital with no significant pleural aspirate obtained. Thus, the tube was removed and patient was referred as a case of suspected pulmonary TB. On past medical history, the patient had been diagnosed with seizure disorder at the same district hospital about 7-months prior to the onset of the chronic cough for which oral

Carbamazepine 200 mg daily was initiated. According to the mother, patient had a normal childhood with no significant medical events and their family history was unremarkable. She was a secondary school student and lived in a rural community with her parents who were peasant farmers growing corn and a variety of vegetables. The patient together with her siblings helped out on their parents’ farm often.

At presentation, we found a chronically-ill looking young female, mildly dyspneic at rest with no pallor, fever or peripheral lymphadenopathy. Chest auscultation was suggestive of left hemithorax consolidation while other systems examined revealed normal findings. Initial investigations done included repeat sputum geneXpert (Negative) and a fasting blood sugar of 5.1mmol. Other test results are shown in Table 1.1 and 1.2.

Chest Computed Tomography (CT-scan) showed replacement of the left lung by a large complex heterogeneously enhancing mass with hypoenhancing areas suggestive of cystic change or necrosis. The lesion caused complete compression of the left main bronchus and partially encased the pulmonary trunk and thoracic aorta (Fig. 2). Oesophageal compression by the mass was also evident. A second 4 mm solitary pulmonary nodule was noted in the apex of the right lung as well as multiple enlarged supraclavicular, paratracheal, sub-carinal, and left hilar lymph nodes.

A Left lung malignant tumor with possible metastasis to the contralateral lung and mediastinal lymph nodes was strongly suspected. We also entertained possible brain metastasis as a cause of the previously diagnosed seizure disorder. Percutaneous lung biopsy was done but histology was inconclusive due to inadequate tissue specimen. The pathologist’s report, however, made note of possible presence of fungal elements which could not be distinguished from artefacts in the absence of special stains. Treating clinicians interpreted this as a possible superimposed fungal infection and initiated a short



**Fig. 2** Initial contrast enhanced axial chest-CT images in mediastinal window showed a huge heterogeneously enhancing left lung mass (long arrows) with extension into the left main stem bronchus (short arrow), vascular encasement and mediastinal shift to the right



**Fig. 3** Pictures showing the anterior chest wall mass proximal to the right breast (a) and posterior chest wall masses (b)



**Fig. 4** Posterior and lateral chest wall mass with an ulcer at old chest tube insertion site in image (a). Image (b) shows interval reduction in the size of the mass

course of oral fluconazole 200 mg daily. Repeat biopsy was arranged on out-patient basis due to insistence by her parents for discharge.

Patient unfortunately defaulted on the biopsy appointment and returned to clinic about five months later with symptoms of dysphagia to solids, focal seizures of the left upper limb (defaulted on carbamazepine) and huge lumps on her left chest wall. She was fully conscious with no lateralizing signs but looked cachexic (Her weight had dropped from 52 kg at initial visit to 36 kg), pale, afebrile and moderately dyspnoeic at rest. The chest lumps/

masses were firm-to-hard, non-tender and located on the left anterior, lateral, and posterior chest wall with the largest measuring 15×25 cm (Figs. 3a and b and 4a) with no differential warmth. An ulcer discharging a gelatinous fluid at the old chest tube insertion site was noted (Fig. 4a) and the spleen was palpable 5 cm below the costal margin.

Abdominal ultrasound confirmed splenomegaly (15.8cm) with nonspecific multiple cystic and tubular lesions within it and a diffusely enlarged liver (18cm). The suspicion of a primary lung malignancy with brain

and contralateral lung metastasis was maintained and repeat percutaneous lung biopsy performed. Histology revealed rounded and buckled yeast forms; one with a narrow-based budding yeast emerging and the other with pale-staining rounded and buckled yeast-like organisms on Grocott stain and mucicarmine stains respectively (Fig. 5a and b). No malignant cells were noted.

A diagnosis of pulmonary cryptococcosis with a giant cryptococcoma in the left lung and a small cryptococcal granuloma in the right lung was secured. Though we were unable to get a brain CT-scan due to financial constraints, dissemination to the brain cortex was strongly suspected based on the focal seizures. There was also dissemination to the spleen and mediastinal lymph nodes. Serum CrAG testing was not immediately accessible, and a lumbar puncture was not done due to the huge posterior chest wall masses and its attendant difficulty with positioning. A 2-week induction phase was initiated with Amphotericin B deoxycholate 1 mg/kg on day 1 followed by 1.5 mg/kg daily and oral Fluconazole 400 mg twice daily. While on amphotericin therapy, she developed severe hypokalemia and hyponatremia that required electrolyte correction. She also required blood transfusion due to associated severe anemia. Upon successful completion of the induction phase, high-dose fluconazole 400 mg twice daily was continued for the consolidation phase. Progressive reduction in the size of the chest wall masses based on periodic chest circumference measurements was noted (Fig. 4b). Patients' symptoms of cough and dysphagia was improving and focal seizures controlled on oral Levetiracetam.

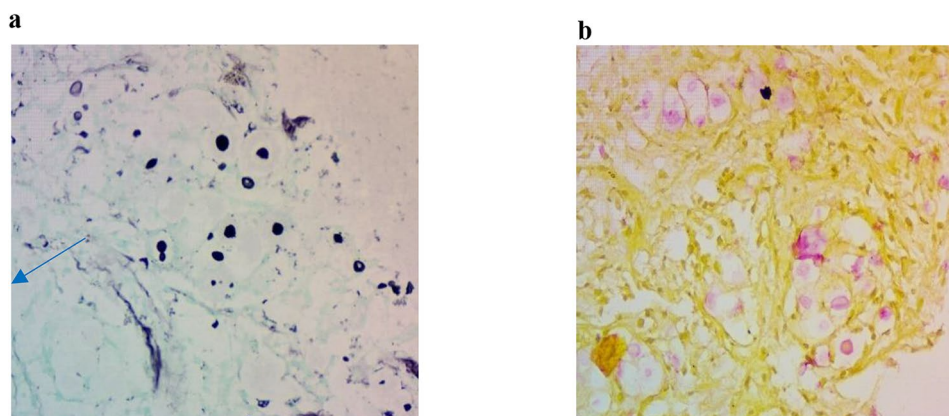
Patient was successfully discharged after 64 days on admission and was scheduled for a review within 2 weeks. The decision was to refer to thoracic surgeons if reduction in size of cryptococcoma was not significant on the anti-fungal therapy. Patient defaulted clinic review again for unclear reasons and a follow-up call to parents' revealed patient had passed away at home about 6 weeks

post-discharge following an acute episode of breathlessness after a large meal.

## Discussion

Pulmonary cryptococcosis, though rare, has been shown to occur more in the immunocompetent in whom the presentation tends to be atypical, and diagnosis delayed as most cases are asymptomatic and identified as incidental lung nodules or lung cancer (6, 7, 8, and 11). Our case was presumed immunocompetent as screening for common causes of immunosuppression such as HIV and diabetes were negative. We also had a low index of suspicion for possible primary immunodeficiency state due to the absence of any history of ill-health or recurrent infections during childhood or early adolescent period. Although not very apparent, our patients' intermittent work on her parents farm may have exposed her to cryptococcal spores typically found in the soil, bird's droppings, decaying woods and on trees.

Where symptoms do occur in PC, they are mild and non-specific and may include cough, chest pain, weight loss, fever or hemoptysis. The extent and severity of cryptococcal infections has been shown to be dependent on the level of immunity and this explains why the disease is predominantly localized to the lungs in immunocompetent patients, as opposed to the rapid dissemination from the lungs to the brain/meninges with no or insignificant lung lesions in the immunocompromised host [7]. In the current review, the patient similarly had a chronic cough but only sought medical help when she began experiencing shortness of breath. We however suspect on hindsight that the earlier diagnosis of a seizure disorder months prior to the onset of the chronic cough, could have been the first evidence of the disease in this young female. This is an example of how pulmonary disease in the immunocompetent could remain subclinical for months and may only present with symptoms of dissemination. As similarly reported by Suwatanapongched et al., 67% of the



**Fig. 5** **a**: Photomicrograph. (Grocott stain X400) showing rounded and buckled yeast forms (arrowed). **b**: Photomicrograph (Mucicarmine stain X400) showing pale-staining rounded and buckled yeast forms (arrowed)

immunocompetent patients diagnosed with PC already had CNS dissemination attributed to delayed diagnosis which allowed for disease advancement [12].

Radiologically, pulmonary cryptococcosis in the immunocompetent typically presents with solitary nodules/masses averagely 0.5–52 mm in size, mostly peripheral in the upper to middle lung zones, hence commonly misdiagnosed as PTB or lung cancer when solitary [5, 6, 11]. On the contrary, some reports have shown that the size of cryptococcal nodules/masses could vary widely ranging from 1 cm to 15 cm in its widest diameter [12]. The cryptococcal mass in our patient was huge, invading and outgrowing the left thoracic cage with multiple areas of cystic change. Mitsuoka and Kanazawa similarly reported a case of a giant cryptococcoma characterized by cystic areas with chest wall invasion noted on CT-scan [13]. The rare presence of mediastinal and hilar lymph node enlargement as well as compression of vascular structures within the mediastinum, which our patient had, are considered atypical in PC and indicative of an aggressive disease [12, 14]. The rapid growth of the cryptococcal mass in our patient with significant invasion of the chest wall within 5-months from the initial presentation is another evidence of the rarely aggressive nature of PC, characteristically known to run an indolent course.

Diagnosis of cryptococcosis usually begins with a high index of suspicion in an immunocompromised patient such as in HIV, promoting early disease recognition. The infection in an immunocompetent patient is on the contrary hardly suspected, resulting in extremely delayed diagnosis as evident in the current case report in whom the disease was not even considered as a differential. The diagnosis was only secured by the histopathological presence of cryptococcus in the specimen obtained. Non-invasive diagnostic tests such as serum cryptococcal antigen (CrAg) has been shown to have a high sensitivity in diagnosing disseminated cryptococcal infections not only in the immunocompromised host, but also in the immunocompetent, especially in those with diffuse or prominent lung lesions as in our patient [15, 16]. Should we have had the disease on our list of differentials, a test for serum CrAg could not only have clinched the diagnosis much earlier but would have exposed the occult CNS dissemination. Current guidelines therefore recommend mandatory serum CrAg testing in immunocompetent patients with PC for early detection of disease dissemination [17]. This ensures appropriate treatment with IV amphotericin B+flucytosine (preferred) or high-dose Fluconazole rather than only oral anti-fungal therapy recommended in cases of isolated PC [17]. In our situation, the unavailability of flucytosine and the high cost of Liposomal Amphotericin B led to the choice of Amphotericin B deoxycholate (lipid complex) in combination with oral Fluconazole 400 mg twice daily.

As per current guidelines, anti-fungal therapy is the recommended first line therapy for all cases of PC with surgical intervention vaguely reserved for cases with poor response to initial anti-fungal therapy [14, 17]. There was appreciable response in our patient when initiated on anti-fungal therapy and this was evident in size reduction of chest wall masses noted in Fig. 5b. There was also significant symptom improvement, particularly with the dysphagia. Patients' death post-discharge was unexpected and our suspicion of the cause of death was possible aspiration pneumonia, judging from the event surrounding her death. Could this have been a result of significant intrathoracic pressure or raised intracranial pressure from a further increase in the size of the cryptococcoma in the lung or brain respectively? Though there was objective improvement in the disease prior to her discharge, the patient may have defaulted on therapy considering the erratic clinical course encountered. In a case report by Anandpara and team, the patient similarly had a sizeable lung cryptococcoma with significant mediastinal infiltration and compression of vascular structures but the outcome on anti-fungal treatment was positive. Perhaps, the comparatively larger cryptococcal mass in our case and the possible CNS dissemination (known to be associated with poor prognosis), could have been the differing factor affecting outcome in our patient [18]. In another presentation by Haddad et al., undiagnostic bronchoscopy led to an exploratory thoracotomy and lobectomy in a 17 year old female and PC was confirmed on histology. Post-lobectomy adjuvant anti-fungal treatment based on a positive CrAg test also yielded a favorable outcome [19]. Similarly, in the case by Mitsuoka and Kanazawa, a favorable response to anti-fungal therapy was observed only after a minimally invasive thoracotomy was done with drainage of a discolored fluid from the chest wall-invading cryptococcoma [13]. With the above favorable reports, we pondered on whether an early surgical intervention in combination with anti-fungal therapy could have improved the outcome in our patient.

## Conclusion

With this first documentation in our setting, pulmonary cryptococcosis should be considered as a differential in cases of a lung mass/masses particularly when no clear risk factors for lung malignancy exists. Serum CrAg testing and early involvement of thoracic surgeons should be encouraged in a patient with a giant pulmonary cryptococcoma.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12890-024-03318-w>.

Supplementary Material 1

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### Author contributions

HG - Originator, manuscript writing and prepared radiological imaging. JSAM - Originator, writing of manuscript and preparation of clinical images. SD - manuscript writing and preparation of clinical images. ENA - manuscript writing and gathering of clinical information PP - manuscript writing and preparation of clinical data.

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### Data availability

All data underlying this publication are available as part of the article and no additional source data are required.

### Declaration

#### Consent for publication

Written informed consent was obtained from the parent of the patient for publication including images and pictures therein.

#### Competing interests

The authors declare no competing interests.

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### References

1. Erratum, *Open Forum Infect Dis.* 2017;4(1):ofw218. <https://doi.org/10.1093/ofid/ofw218>. Erratum for: *Open Forum Infect Dis.* 2016;3(3):ofw167. doi: 10.1093/ofid/ofw167.
2. Choi HS, Kim YH, Jeong WG, Lee JE, Park HM. Clinicoradiological features of pulmonary cryptococcosis in Immunocompetent patients. *J Korean Soc Radiol.* 2023;84(1):253–62. <https://doi.org/10.3348/jksr.2022.0008>.
3. Velagapudi R, Hsueh YP, Geunes-Boyer S, Wright JR, Heitman J. Spores as infectious propagules of *Cryptococcus neoformans*. *Infect Immun.* 2009;77(10):4345–55. <https://doi.org/10.1128/IAI.00542-09>.
4. Park BJ, Wannemuehler KA, Marston BJ, Govender N, Pappas PG, Chiller TM. Estimation of the current global burden of cryptococcal meningitis among persons living with HIV/AIDS. *AIDS.* 2009;23(4):525–30. <https://doi.org/10.1097/QAD.0b013e328322ffac>.
5. Fox DL, Müller NL. Pulmonary cryptococcosis in immunocompetent patients: CT findings in 12 patients. *AJR Am J Roentgenol.* 2005;185(3):622–6. <https://doi.org/10.2214/ajr.185.3.01850622>.
6. Zhang Y, Li N, Zhang Y, Li H, Chen X, Wang S, Zhang X, Zhang R, Xu J, Shi J, Yung RC. Clinical analysis of 76 patients pathologically diagnosed with pulmonary cryptococcosis. *Eur Respir J.* 2012;40(5):1191–200. <https://doi.org/10.1183/09031936.00168011>.
7. Setianingrum F, Rautemaa-Richardson R, Denning DW. Pulmonary cryptococcosis: a review of pathobiology and clinical aspects. *Med Mycol.* 2019;57:133–50. <https://doi.org/10.1093/mmy/myy086>.
8. Shi J, Chen J, Hu L, Ma AHY, Hu H, Wang C, Huang J, Song Q, Qian G. Retrospective analysis of pulmonary cryptococcosis and extrapulmonary cryptococcosis in a Chinese tertiary hospital. *BMC Pulm Med.* 2023;23(1):277. <https://doi.org/10.1186/s12890-023-02578-2>.
9. Deok-jong Yoo S, Worodria W, Davis JL, Cattamanchi A, den Boon S, Kyeyune R, Kisebo H, Huang L. The prevalence and clinical course of HIV-associated pulmonary cryptococcosis in Uganda. *J Acquir Immune Defic Syndr.* 2010;54(3):269–74. <https://doi.org/10.1097/QAI.0b013e3181ce6b19>.
10. Gunda DW, Bakshi FA, Rambau P, Kilonzo SB. Pulmonary cryptococcosis presenting as acute severe respiratory distress in a newly diagnosed HIV patient in Tanzania: a case report. *Clin Case Rep.* 2015;3(9):749–52. <https://doi.org/10.1002/ccr3.337>.
11. Eremiev S, Espejo D, Pilia MF, Sempere A, Teresa Martín-Gómez M, Ojanguren I, et al. Pulmonary cryptococcosis mimicking Lung Cancer. *Open Respiratory Archives.* 2022;4(2):100154.
12. Suwatanapongched T, Sangsatra W, Boonsarngsuk V, Watcharananan SP, Incharoen P. Clinical and radiologic manifestations of pulmonary cryptococcosis in immunocompetent patients and their outcomes after treatment. *Diagn Interv Radiol.* 2013 Nov-Dec;19(6):438–46. <https://doi.org/10.5152/dir.2013.13049>.
13. Mitsuoka S, Kanazawa H. Images in Thorax. An unique case of primary pulmonary cryptococcosis with extensive chest wall invasion. *Thorax.* 2005;60(1):86. <https://doi.org/10.1136/thx.2004.031658>.
14. Anandpara KM, Aswani Y, Hira P. Large Solitary Pulmonary Cryptococcoma mimicking lung carcinoma in an Immunocompetent patient. *Malays J Med Sci.* 2018;25(1):114–8. <https://doi.org/10.21315/mjms2018.25.1.13>.
15. Lu Y, Ding M, Huang J, Fu C, Wan Y, Jiang J, Huang J. Clinical characteristics and image features of pulmonary cryptococcosis: a retrospective analysis of 50 cases in a Chinese hospital. *BMC Pulm Med.* 2022;22(1):137. <https://doi.org/10.1186/s12890-022-01930-2>.
16. Min J, Huang K, Shi C, Li L, Li F, Zhu T, Deng H. Pulmonary cryptococcosis: comparison of cryptococcal antigen detection and radiography in Immunocompetent and immunocompromised patients. *BMC Infect Dis.* 2020;20(1):91. <https://doi.org/10.1186/s12879-020-4818-1>.
17. Global guideline for the Diagnosis and management of cryptococcosis: an initiative of the ECMM and ISHAM in cooperation with the ASM. *Lancet Infect Dis;* 2024.
18. Beardsley J, Sorrell TC, Chen SC. Central Nervous System Cryptococcal infections in Non-HIV infected patients. *J Fungi (Basel).* 2019;5(3):71. <https://doi.org/10.3390/jof5030071>.
19. Haddad N, Cavallaro MC, Lopes MP, Fernandez JM, Laborda LS, Otoch JP, Ferreira CR. Pulmonary cryptococcoma: a rare and challenging diagnosis in immunocompetent patients. *Autops Case Rep.* 2015;5(2):35–40. <https://doi.org/10.4322/acr.2015.004>.

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