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Cryptic Clues from an Acute Abdomen: A Case Report of Peritonitis turning into Disseminated Cryptococcosis

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Case Report

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Abstract

Background:

Cryptococcosis is a life-threatening opportunistic fungal infection that primarily affects immunocompromised individuals, most commonly presenting as meningitis. Peritoneal involvement is exceedingly rare and can closely mimic common acute surgical conditions, often resulting in delayed diagnosis and treatment. This case describes an unusual presentation of disseminated cryptococcosis as acute peritonitis with subsequent progression to cryptococcal meningitis; underscoring the diagnostic challenges posed by atypical intra-abdominal infection.

Case presentation:

A previously healthy female homemaker in her late 20s presented with a 20-day history of intermittent low-grade fever, followed by 7 days of right lower abdominal pain and multiple episodes of non-projectile vomiting. Clinical examination revealed right iliac fossa tenderness with guarding and rebound tenderness, suggestive of acute appendicitis with perforation. Her pre-operative laboratory work-up revealed HIV positivity and emergency laparotomy with open appendicectomy and drainage of pelvic abscess was performed. Histopathological examination demonstrated granulomatous inflammation with encapsulated yeast forms consistent with *Cryptococcus neoformans*, later confirmed by special fungal stains. On postoperative day 3, the patient developed headache and neck stiffness. Subsequent evaluation identified disseminated cryptococcosis with cryptococcal meningitis, mesenteric lymphadenitis, and urinary tract involvement, alongside newly diagnosed advanced HIV infection with CD4 cell count of 98 cells/mm^3. The patient received amphotericin B-based induction antifungal therapy followed by prolonged fluconazole consolidation and maintenance therapy. Antiretroviral treatment was initiated in a deferred manner after stabilisation to avoid IRIS related complications. Clinical improvement was observed with resolution of symptoms and significant immunological recovery during follow-up with no residual complications.

Conclusions:

This case illustrates an exceptionally rare presentation of disseminated cryptococcosis manifesting initially as acute peritonitis and later progressing to central nervous system involvement. This is the first reported case where peritonitis precedes systemic involvement and meningitis in cryptococcosis clinically. It emphasizes the importance of maintaining a high index of clinical suspicion for opportunistic fungal infections in atypical or non-resolving intra-abdominal infections, particularly in patients with undiagnosed immunosuppression. Early histopathological recognition, timely antifungal therapy, and coordinated management of underlying HIV infection are critical for improving outcomes.

Introduction

Cryptococcosis is an invasive fungal infection, that predominantly affects immunocompromised individuals, especially in advanced HIV infection with CD4 count less than 100cells/microL. Despite widespread

antiretroviral therapy, cryptococcal meningitis remains a major global health problem and a leading cause of AIDS-related mortality worldwide.[1] In contrast, peritoneal involvement is an exceptionally rare manifestation in HIV-positive patients and is most commonly reported in those with cirrhosis or on peritoneal dialysis.[2] Cryptococcal peritonitis often closely mimics spontaneous bacterial peritonitis with nonspecific symptoms, and initially negative ascitic fluid studies; leading to delayed diagnosis.[3]

Case Report

A female homemaker in her late 20s, presented with right lower abdominal pain for 7 days and multiple episodes of non-projectile, non-bilious vomiting one day prior to admission. She had a 20-day history of low-grade intermittent fever. The abdominal pain was sharp, aching, localized to the right lower quadrant, without radiation or diurnal variation and worsened with ambulation. She reported associated anorexia and sleep disturbance. There were no urinary, gastrointestinal, respiratory complaints or history of weight loss. Her menstrual history was also regular, and her family history was unremarkable. She had no comorbidities and denied any habits. On physical examination, she was found to have rebound tenderness in the right iliac fossa with guarding.The prolonged episode of fever preceding abdominal symptoms prompted consideration of a broad differential diagnosis, including systemic, gynaecological, and urinary causes, which in reproductive-age women can often mimic an acute surgical abdomen.

Normal serum β-hCG levels ruled out any ectopic pregnancies, but her pre-operative serology revealed HIV positivity. Since she was hailing from a region endemic to Leptospirosis, acute febrile illness profile was done to rule out any underlying infections. The absence of raised intracranial pressure signs, headache, focal neurological deficits and a preserved Glasgow-Coma-Scale score made primary meningeal infection unlikely. In the absence of genitourinary symptoms, appendicitis, with possible perforation was considered as the leading differential diagnosis. Gastroenteritis was deemed less likely due to the absence of diarrhoea and the localisation of pain to the right lower quadrant.

These findings were corroborated by ultrasonography abdomen, which revealed free fluid in the pelvis, and probe tenderness in the right iliac fossa. In view of suspected intra-abdominal sepsis, the patient underwent emergency laparotomy with open appendicectomy and drainage of a pelvic abscess.

During surgery, the pus was collected and sent for culture and sensitivity; omental biopsy and appendix specimen was sent for Histopathological examination. Histopathology revealed transmural granulomatous inflammation with fungal spores (Supplementary Figure-A). For confirmation, special stains Grocott methenamine silver (GMS) and Periodic Acid-Schiff (PAS) were positive showing oval/round yeast cells with polysaccharide capsule and characteristic halo, suggestive of cryptococcal appendicitis (Supplementary Figure-B, C). Diagnosis of Histoplasmosis was excluded as mucicarmine stain was negative. Thus, microbiological and histopathological examination demonstrated the presence of cryptococcal spores, confirming a diagnosis of cryptococcal appendicitis.

Urine routine showed 2 to 3 pus cells and yeast like budding cells. PAS stain done in urine sample was also positive indicating cryptococcuria (Supplementary Figure-D).

On post-operative day 3, patient developed headache, thus the next goal was to rule out and limit any systemic infection. Examination revealed neck stiffness without focal neurological deficits, and fundus examination was normal. CT brain was unremarkable. Lumbar Puncture and Cerebrospinal Spinal Fluid (CSF) analysis revealed a total cell count of 50, all lymphocytes. CSF-CBNAAT (Cartridge-Based Nucleic Acid Amplification Test) was negative for Tuberculosis. However, India Ink staining was positive and *Cryptococcus neoformans* was grown after 48 hours of incubation, confirming the diagnosis of cryptococcal meningitis. CD4 count was 98 cells/mm^3.

MRI Brain with contrast showed cryptococcomas. CECT abdomen done in view of persistent drain output on post operative day 9 showed multiple enlarged mesenteric lymph nodes. Subsequently, with the presence of cryptococcuria, disseminated cryptococcal infection was confirmed.

Treatment and Outcome

Patient was started on induction therapy of intravenous amphotericin B 50mg (1mg/kg) daily for 10 days, along with mannitol and dexamethasone. Cotrimoxazole double strength tablet once daily was started for Pneumocystis pneumonia prophylaxis. Due to unavailability of flucytosine, amphotericin B was followed by oral fluconazole 1200 mg daily for 7 days.

Repeat Lumbar Puncture done after 14 days of amphotericin B treatment showed persistent India Ink positivity. Following up, fluconazole 800mg over 2 doses daily was continued for 8 weeks.

The patient was put on fluconazole continuation therapy 200mg daily for 12 months and then finally stopped. Anti retroviral therapy was started 8 weeks after the starting of anti-fungal therapy to minimise any potential Immune-Reconstitution-Inflammatory-Syndrome(IRIS) related complications.

After 12 months, the patient has stabilised significantly (CD4 count 211 cells/mm^3) while there were no lasting artefacts of this episode. Her CD4 counts were followed up regularly every 3 months and there was steady rise in trend, with no complications. (Fig-1)

Discussion

C. neoformans is an encapsulated yeast with a thick polysaccharide capsule (visible as clear halos while staining) and melanin-rich cell wall. The key virulence factors are the capsule which inhibits phagocytosis, and melanin which provides protection against oxidative stress. Typically, infection begins by inhalation of spores, establishment of a latent pulmonary focus, while in immunocompromised hosts the fungus can disseminate hematogenously, often involving the central nervous system. [[3],[4],[5]]

Although the use of Highly-Active-Antiretroviral-Therapy has significantly lowered the incidence of cryptococcosis, the estimated global burden of HIV associated cryptococcal meningitis still approximates 1 million cases annually worldwide.[6] While this number is staggering, Cryptococcus most commonly manifests as meningitis or pneumonia, and Cryptococcal peritonitis remains an extremely rare manifestation. A literature review identified 61 cases over six decades, majority of which were associated with primary immune deficiency; 19.7% of them being HIV/AIDS, with liver cirrhosis leading the list.[2] In patients with cryptococcal peritonitis, concomitant CNS and urinary involvement was reported in 16.4% and 8.2% of cases,

respectively.[2] Therefore, cryptococcal peritonitis should be included in the differential diagnosis of peritonitis, especially in patients with concomitant immunocompromised states.

Clinical manifestations of cryptococcal peritonitis are very nonspecific and often mimics spontaneous bacterial peritonitis.[3] Patients typically present with fever, abdominal pain or distension, and worsening ascites. In many cases, in ascitic fluid analysis neutrophils predominate initially (just like Spontaneous Bacterial Peritonitis), but a higher lymphocyte percentage than a typical bacterial peritonitis is often a subtle clue. If bacterial cultures remain negative after 48 hours (and particularly if the patient is not improving on empirical broad-spectrum antibiotics), it should prompt suspicion of an underlying fungal peritonitis.[[3],[7]] Importantly, if neurological symptoms or high clinical suspicion occur, evaluation for cryptococcal meningitis is indicated, as CNS dissemination often accompanies disseminated disease and has significant prognostic implications.[3]

Diagnosis of cryptococcal peritonitis begins with prompt diagnostic paracentesis in at-risk patients. Ascitic fluid should be examined with appropriate fungal stains, cryptococcal antigen testing, and culture.[[3],[8]] Once cryptococcal infection is suspected or confirmed, further evaluation for dissemination, including serum and cerebrospinal fluid (CSF) analysis should be done, guided by the clinical scenario.[[3],[9]]

Current treatment recommendations for cryptococcal meningitis and disseminated cryptococcosis are outlined in two major guidelines. (Fig. 2)[[10],[11]] Both recommend an initial 2-weeks induction phase. If CSF cultures remain positive at the end of induction therapy, reinitiation of an additional 2-week induction course can be considered. This is followed by an 8-week consolidation phase with high dose oral fluconazole; then a prolonged maintenance phase with oral fluconazole for atleast 6–12 months until immune recovery is achieved, cryptococcal antigen becomes negative, and relapse risk is minimised. Liposomal amphotericin B is preferred, while amphotericin B deoxycholate remains as an alternative in resource-limited settings. If flucytosine is unavailable, fluconazole alone may be used, although recent evidence suggests lower resistance rates and improved outcomes when fluconazole is combined with flucytosine.[[10],[11]] Due to drug unavailability and resource limited conditions, the initial therapy had to be modified from the standard regimen, with high-dose fluconazole added one week later during induction period. Although India ink staining remained positive at two weeks, re-initiation of induction therapy was withheld because the patient showed rapid clinical improvement. Afterwards, the consolidation and maintenance therapy were continued according to standard guidelines. This initial change was effective and did not affect the outcome as evidenced by the subsequent uncomplicated follow-up period for the patient.

In conclusion, cryptococcal peritonitis is a rare but potentially life-threatening manifestation of disseminated cryptococcosis. It should be considered in immunocompromised patients with ascites who fail to respond to standard antibacterial therapy. Atypically, it can present initially as peritonitis and later progress to more commonly encountered meningitis variant, thus its important to be wary of dissemination. Additionally, although lymphocytic CSF in India primarily points towards Tuberculosis, Cryptococcus and Listeria meningitis should be kept as differentials specially in immunocompromised patients.

Declarations

Ethics approval and consent to participate- Approval was obtained from Institutional Ethics Committee of Kasturba Medical College, Mangalore, MAHE, India, Protocol No.- IECKMCMLR 04/2026/187

Consent for publication- Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of the journal.

Availability of data and materials- Not applicable

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Authors' contributions- AB, AMV, VKK were involved in the clinical care and treatment of the patient. SP prepared the manuscript. All authors read and approved the final manuscript.

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Patient perspective:

When I first developed fever and headache, I thought it was a cold, but it stayed for a long while. I started developing pain in my abdomen and took antacids. But suddenly one day the pain really increased, and it was difficult to move, I could barely stay awake. My family members brought me to the hospital and doctors told me I had to get operated urgently; they needed to remove liquid from my abdomen. I was scared as I was not prepared for such things, but my family and doctors calmed me down. They told me I had HIV, but I realised it much later, and when I did, I was devasted thinking I cannot live, but more what everyone will think of me. I did not want to speak with my family, but the doctors helped us talk after one day. I was relieved when my family supported me but there were still some doubts at that time. I'm now going to therapy and taking medicine regularly to live better.

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Figures

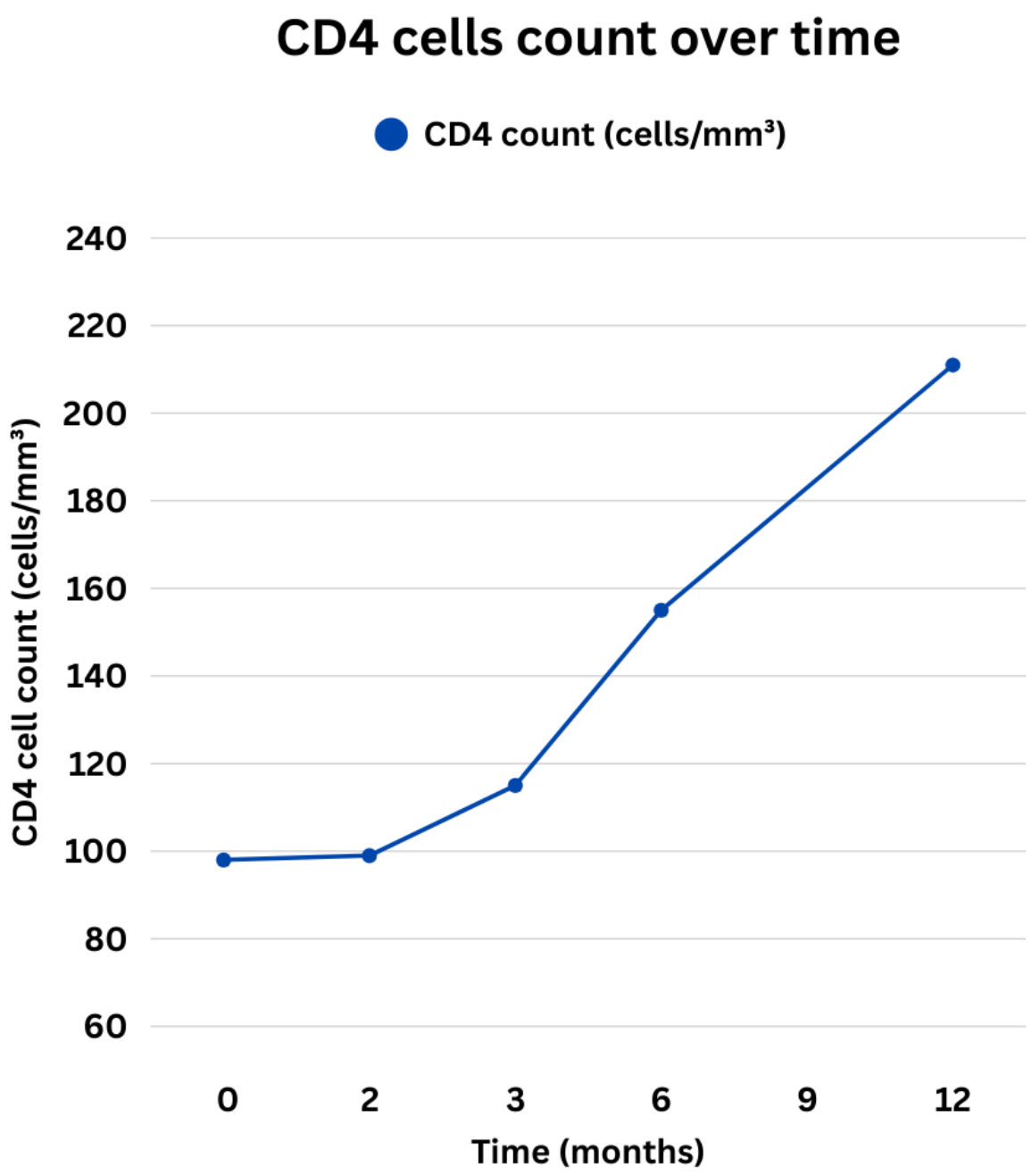


Figure 1

CD4 cell count over 1 year follow-up: Rising trend of CD4 cells over a year; note the CD4 cells did not rise significantly till anti-retroviral therapy was initiated and their values (cells/mm³) were 98 at presentation, 99 after 2 months, 115 after 3 months, 155 after 6 months, 183 after 9 months and 211 after 12 months follow-up

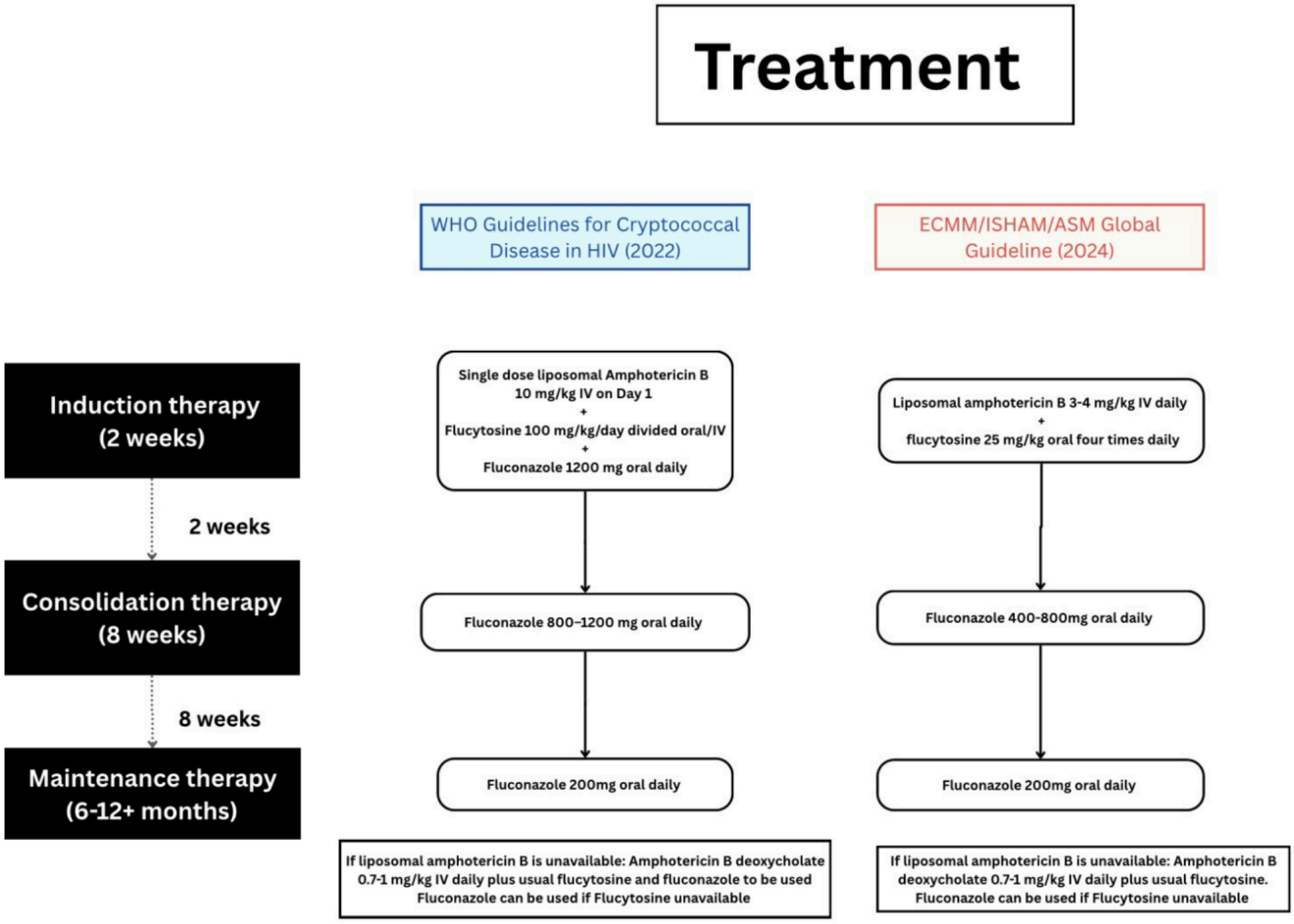


Figure 2

Treatment protocol for Cryptococcal meningitis and disseminated cryptococcosis: Both WHO guidelines for Cryptococcal Disease in HIV 2022 and ECMM/ISHAM/ASM Global Guideline 2024 are listed [[10,[11]]

Supplementary Files

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